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NUTLEY NEW JERSEY

THE AMERICAN
JOURNAL OF PHARMACY

VOL. 102 APRIL, 1930 NO. 4

EDITORIAL

POISON RUM FACTS

THE "SPECIAL CONTRIBUTOR" on the staff of this JOURNAL has often declared in its pages and elsewhere that the claim that illicit liquor is doing special harm is unfounded. Very little attention has been paid to his statements. Newspapers are primarily interested in sensations. The words "poison rum" make striking headlines. Opponents of Prohibition find much comfort and tactical advantage in claiming that the present situation leads to the sale of impure liquors, responsible for many deaths. It is noticeable, however, that very few deaths are ascribed to other substances than alcohol in liquors in the reports of coroners or courts. Some time ago the Director of Public Safety in Philadelphia made a newspaper proclamation that much poison rum was being sold in the city. The editor of a newspaper that had published the statement, and made editorial allusion to it, was asked to secure from the city laboratory the analytic data upon which the Director's statement was based. No assistance was rendered. The editor simply replied that the Director had given the newspaper from time to time information as to analyses, but apparently this was not for publication.

Chemists having large experience in examination of confiscated liquors (Lythgoe of Massachusetts, Howard of New Hampshire, Bailey of Connecticut) have reported that a very small proportion of all the samples tested have been found to contain anything not in standard liquors. Some years ago, Doran and Beyer reported to the American Public Health Association the results of analyses of about 70,000 samples of confiscated spirits examined in the laboratory of the Internal Revenue Department. They found no ingredient not present in standard spirits, but in a few cases a notably large amount of alde-

hyde. They suggested that this might have a poisonous action, but the data submitted did not in any way bear out their contention. Aldehyde, by the way, exists in apple juice, so that if it is seriously injurious in small amount, it might be said that "an apple a day" will not keep the doctor away but bring him.

Within the past few days an interview with Dr. Doran (now, as is well known, in charge of the Prohibition Administration) has been published in the *Popular Science Monthly* (May, 1930). The report is from the pen of the distinguished and experienced chemist, Dr. E. E. Free. It will be of interest and value to set forth some sentences from this report, which, of course, are Dr. Doran's definite statements.

There is great outcry at present about "synthetic gin," yet seldom has America seen anything else. Real gin is generally supposed to be made by fermenting the berries of the juniper and distilling the product, just as whisky is made by fermenting and distilling a "mash" of water and grain, or brandy by fermenting and distilling grape juice, or rum by fermenting and distilling a mixture of sugar and water. That was the theory about gin.

Once, before prohibition, I tested (being then a practicing chemist) one bottle of gin which apparently had been made in that way. But then, as now, virtually all the gin drunk in America, no matter how foreign and pretentious the label, was made synthetically out of juniper oil, other flavoring matters, and alcohol. The blending, it is true, was better than now and sometimes the blended product was redistilled or aged to improve the flavor; refinements which the present-day industry has not yet reached. But all American gin, practically speaking, was just as "synthetic" fifteen years ago, before prohibition, as it is today.

Also it was very little more wholesome, for one thing that the present well-organized bootlegging industry has learned is that it is not good business to poison one's customers. Little of the booze now on the American market is really unwholesome, assuming that any booze is wholesome.

Probably there were about as many instances of poisoning from bad liquor in preprohibition days as now. At present, at any rate, it is chiefly not poisons but *alcohol,* just the same as it always was, that sends heavy drinkers to the hospitals and the casualty lists.

Quod erat demonstrandum.

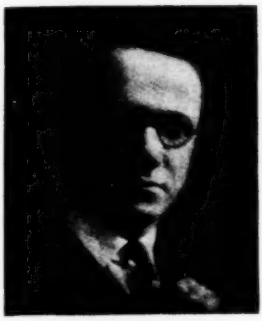
HENRY LEFFMANN.

ORIGINAL ARTICLES

IODINE—THE "ELEMENT OF DOUBT"*

By Ivor Griffith, P. D., Ph. M.

THE YEAR 1776 infected a great many people with notions of independence. Jean Baptiste Courtois, a volatile Frenchman, citizen of Dijon, was one of them. For years he had served as valet to a wealthy family in the suburbs of Dijon. In 1776 his former neighbor, Guyton de Morveau, offered him a job as general factotum in his chemical laboratory at the Academy of Dijon. Courtois, familiar with army titles, may have thought that a "general factotum" ranked highly. He soon learned, however, that in the language of the laboratory, a "general factotum" meant nothing less than chief cook and bottle washer.



Ivor Griffith

Yet he stuck to his new job for several years. His employer, Guyton de Morveau, had been Courtois' neighbor and boyhood chum. Only—while Courtois had early entered into family service, his chum had gone to school to study law. And soon he had opened his law office.

Every day in every way he seemed to grow wiser and wiser, busier and busier, richer and richer. And his friend Courtois envied him—envied him still more so when he learned that De Morveau, alive to the fashion of the day, had installed in his home a full fledged chemical laboratory.

For in the best circles of France, in those days, torturing chemicals with fire was a very stylish hobby. Indeed so enamored did De Morveau become of his new avocation, that he began to neglect his law practice and his friends began to worry about his future.

Until—until one Monday morning they read with amazement an announcement which appeared in glaring headlines in the front page of the Dijon *Daily News* to the effect that Guyton de Morveau

*One of a Series of Popular Science Talks given at the Philadelphia College of Pharmacy and Science, 1930 Season.

had been elected by the Board of Trustees of the Dijon Academy to the important post of Professor of Chemistry.

Now in those days a Professor of Chemistry had unlimited possibilities. He could say most anything about Chemistry—and no one knew whether he was right or wrong. And he was no fool specialist—for every field of chemistry was his pasture.

THE LAWYER PROFESSOR

And so Guyton de Morveau deserted the cause of justice and became Professor of Chemistry, Organic, Inorganic, Synthetic, Analytic, Forensic, Physical, Colloid, Pharmacological, Physiological and every logical and illogical kind of chemistry, then known, unknown, practiced and promised.

Of course, so little of chemistry was understood in those days that a lawyer, with a good flow of language, could so well dilute a little knowledge with his flood of words, that a Board of Trustees could be easily fooled. But De Morveau did better than that. Indeed he became a still greater chemist and professor than he was a lawyer —and his name will live so long as chemistry lives—not because he gave Courtois, the elder, a job in his laboratory, but because of the many discoveries he made for himself and for posterity.

Although a little way from our subject, of interest perhaps, will be a brief discussion of the status of the science of chemistry in the days of Professor de Morveau, that is, admitting that such chemistry as was then known deserved the title "science."

Still, one wonders if a century hence, the same may be said of the chemistry of 1930—and its chemical professors and its chemical performances. For as truly as we think we have cause to marvel today at our ninety-two elements and their million combinations, and at our so-called chemical progress—so truly will some fresh popular lecturer on Wednesday evening, February 19, 2030, when we will all be silent in dust, laugh publicly at our ignorance, and wonder why we had failed to see what to him, then, will be ever so obvious—and why we had failed to understand what to him, then, will be ever so evident.

The chemistry of 1776 still bore the mark of the alchemists, those queer quacks who mixed religion with their experiments, and scratched the sign of the cross on all their utensils. In justice to these old fellows however, it might be said that the two great riddles which they so long and so vainly sought to solve, are still unsolved, in spite of split atoms and loosened electrons. Their "philosopher's

stone," wherewith they hoped to change the baser elements to gold—and their "elixir of life" with which they fain would find perennial youth are still elusive mysteries.

Some may have thought that the *Philosopher's Stone* had been found in Wall Street—but remember November. And the nearest we have ever come to the *Elixir of Life* can only be had on prescription.

THE GUESSES OF THE GREEKS

It had taken over a thousand years to upset the guesses of the Greeks that all matter was composed of four elements managed by a fifth—the quintessence. Air, earth, fire and water constituted the quartette—life was the band-master—the quintessence.

But in the days of which we write the vapid mist which had so long pervaded the field of chemistry was beginning to condense on the cold dome of research and reason—and observers were just beginning to contemplate the vast domains before them.

A dozen or two of the elements had been discovered—and the old quartette of the Greeks forgotten. *Air* was now known, thanks to Scheele and Rutherford, as a mixture of oxygen and nitrogen. *Fire* was recognized by Rumford. *Water* was soon thereafter analyzed by Lavoisier and synthesized by Cavendish—and *Earth* was full of possibilities.

The Tria Prima of Paracelsus, too—and the fashionable phlogiston theory had been explained away willingly or otherwise by Geoffroy, the French apothecary, and Priestly—the Lancaster County preacher. And it had come to pass that element hunting was now the popular pastime of Europe's elite.

But let us now return to Courtois and the Professor. Through the latter's influence the erstwhile valet and general factotum secured a new post as manager of a saltpeter factory. Now in those fighting days the saltpeter business was a busy business, for niter was an ingredient of gunpowder—and tons of this pleasing commodity were being daily used to reduce to a minimum and to poverty, the population of certain parts of Europe.

IODINE—BORN 1812

To this saltpeter factory for a little time came his son Bernard—and this is the Courtois whose name will be associated with chemistry as long as chemistry persists. For it is he who is credited with the discovery of Iodine,

that evanescent element, that friendly element, that popular element, which of all the solid elements of universe least likes to live in loneliness.

Early in life Bernard Courtois was apprenticed to Fremy, pharmacist at Auxerre, after having had a short preliminary training at the Polytechnic. Serving in the war of 1799, he later joined Thenard. This is the famous apothecary who discovered hydrogen peroxide—and so made it possible for gentlemen to have their preferences.

Still later we find him with Sequin, who is remembered for his researches with opium and cinchona. Here in 1802 he isolated a crystalline compound from opium, no doubt morphine, but a peculiar timidity inherent in all his performances, kept him from announcing its discovery.

And a few years later Sertürner (1815), an apothecary of Einbeck,* earned an everlasting name when he proclaimed to the world the independent discovery of morphine—and thus achieving to a distinction which might have been Courtois' had his timidity complex not ruined his chances.

A CHANCE ACQUAINTANCE

On the death of his father Courtois retured to his niter factory. There it was, in 1812, while washing the ashes of seaweed which were used as a potash source, and destroying certain impurities with vitriol, that he first noted the violet fumes which later revealed to him iodine—a substance which, on condensing, caked upon and corroded his pans.

His discovery was communicated through his friends to the Institute in Paris. Gay-Lussac, Ampere and Chaptal further studied the new substance which neither Courtois nor his friends had actually called an element.

It so happened just about this time that Sir Humphrey Davy, with a special permit from Napoleon, enjoyed the freedom and perhaps the follies of Paris—and went about its learned circles grasping eagerly at every novel act and thought. He was told of Courtois' violet vapor and he at once suspected it to be elemental in nature and was soon able to confirm his suspicions. Gay-Lussac too, simultaneously arrived at the same conclusion, and submitted his findings in a paper read before the Paris Academy just a few shopping days before Christmas, 1813.

*The little town that gained renown for its far-famed beer, the *Bock*.

Thereupon, so we are told, but not by Sir Davy's biographer, that the versatile Englishman Davy and the volatile Gay-Lussac of France, entered into a strenuous wordy battle as to the priority of their discoveries—the poor apothecary's clerk of Dijon and his saltpeter factory for the time, being, completely ignored. In France, Gay-Lussac had the victory. In England, Davy won.

However, all chemical authorities today honor Bernard Courtois, not Davy, nor Gay-Lussac, for the discovery of the ever important sublimable element *iodine*. Davy has credit enough with his lamp, and Gay-Lussac with his law—let alone the discovery by the former of chlorine, of sodium, of potassium, and by the latter of many fundamental laws of the science.

IODINE—BAPTIZED

To Davy however, goes the honor of having baptized this chemical infant, iodine. The name he chose is derived from the Greek word (ιωδης) meaning violet-like, and which itself is compounded from two Greek words ιον (a violet) plus ειδος (form)—the Latin *viola* being a corruption of the Greek. Thus it is seen that because of the color of its vapor, iodine is named after the modest violet, whose perfume constituent is quite properly called ionone.

Etymologically it is interesting to note in passing that the word iodine has a common ancestry with the word idol and idyll.

Rather true to type was Courtois' death. Like many another pioneer and benefactor of humanity, he died a pauper—the dawn of peace having ruined his saltpeter business, and the six thousand francs which the Academy of Science had awarded him for his discovery having been vainly spent trying to redeem his failing business.

Iodine belongs to that class of simple elements, captained by hydrogen, and thus, unlike its cousin chlorine, exhibits no isotopes. Because of its special salt engendering and other properties, it is grouped in that famous chemical quartette the halogens, chlorine, bromine, fluorine, being the other three members. Of the four—iodine is the only solid, fluorine and chlorine are gaseous, and bromine a heavy liquid.

It is interesting to note here that one of the two remaining undiscovered elements is known to have such chemical properties as will bring it into the halogen group. Just now it is called No. 83—for lack of a better name.

IODINE—AT HOME

America draws most of its crude iodine from one source—Chile, where iodine occurs as sodium iodate associated with crude nitrate of soda or caliche. This source of supply is ample to fill all of America's present need for the element. In Japan a hundred tons are annually produced as a by-product in potassium chloride manufacture from kelp or seaweed, half of which is exported to Russia.

Java has recently come to the fore as a potential source of iodine. Copper iodide an ore native to that country, is now on the free list of the proposed tariff bill, and Javanese iodine may be soon in competition with the Chilean product.

Another source that promises much are the brine wells of the oil producing regions. In Sand Springs, Colorado, an American company has been organized to recover the iodine from this origin. This has been done abroad, both in Russia and in northern Italy.

More will be said later of its widespread occurrence in nature. Here we are only concerned with commercial sources of the element. One of the strange facts connected with the imports of iodine to this country is that nearly three times as much iodine (711,291 pounds) was imported into this country in 1926, as compared with 1925 (246,474 pounds). In 1927 nearly a million pounds were brought in.

THE ABUSE OF IODINE

The startling statement recently made by a drug journal is that this sudden increase was totally due to the fact that tincture of iodine made with alcohol and iodine, was bought in tremendous amounts by bootleggers for the purpose of recovering the alcohol from it for use in alcoholic beverages.

And what a fine source for a Martini!

Further proof is given by noting that the imports have declined since 1928, when the Prohibition Department got on to the iodine trick.

IODINE OWNS PROPERTIES

Iodine, in spite of its vaporous inclinations—in spite of its tendency to be "up in the air" at the least provocation, is a heavy element, having a specific gravity of 4.66. In appearance it is a bluish black, brittle material, having a metallic luster, and a distinctive, disagreeable odor.

It is not very soluble in water, one part of it dissolving in 2950 parts of water, or about 20 grains to the gallon. Such a solution is

however, not permanent, and particularly so when light is permitted to act upon it. With alcohol and water its solutions are amber colored—with chloroform it shows its true molecular color—violet.

When heated to 114 degrees C. iodine fuses, becomes liquid, and then immediately gathers together its molecular cohorts and begins a large scale migration. Away from the heat its particles go, and only rest when they come to a cooler climate. This is the process of sublimation, and thus is iodine purified.

Its vapors have a beautiful violet color. I do not know whether its emission of these violet radiations has anything to do with its chemical restlessness—certain it is that the wave lengths of light on the violet end of the spectrum are busier chemically than those toward the red end.

Indeed the iodine color scheme is quite diversified. Because of its reactivity with starch, producing as it does a vivid bluish black, it is used as a starch re-agent. A peculiar behavior of this starch iodide is the evanescence of its color. Under the influence of heat the bluish black disappears, only to return again when cooled. Hyposulphite of soda readily dissipates this color, hence its use in removing such stains from starched garments.

With mercury, iodine shows a range of colors from yellow to green to red, depending upon the proportions of the elements. Thus mercurous iodide may be green or yellow, and the mercuric iodide a scarlet red.

One of the most striking of the colored iodides is that of cobalt (cobaltous iodide CoI_2), which in a 15 per cent. aqueous solution becomes red at 10 degrees C., and on rise of temperature exhibits every shade of color from red to olive green.

As I have previously mentioned, iodine is a capricious element. Where it exists in a state of single blessedness it evidences a great unrest—its molecules always on the go—ready at the slightest hint of hot weather, to migrate elsewhere to a cooler climate. Of all the solid bachelor elements, none is so restless as iodine.

Even when wed to another element, iodine rarely honors its vows. In almost every instance the old wanderlust returns. Consider the union of iodine and nitrogen in the form of nitrogen triiodide. Nitrogen, the lazy element, and iodine the volatile, can be united—but not for long. Nitrogen is so fond of freedom—so atomically lazy that it nearly always brands its compounds with a wicked reputation—wicked because of their explosive inclinations—

and explosive because of nitrogen's perennial desire to return to its state of laziness.

Cotton of itself is a sedate vegetable fiber, but let it once be tied to nitrogen the lazy, and oxygen the busy—and it becomes at once the fiery rascal gun cotton. Glycerin the mild, changes its name to dynamite when it weds the nitrate radical.

BANG!!

Now then, what can be expected when iodine the restless, marries this explosion-loving nitrogen! The result of such a union is just what one would expect. The finicky nitrogen tri-iodide, a compound so anxious for explosion that one only has to tickle it with a feather to incite it to violent argument.

This compound nitrogen tri-iodide is the popular metastable chemical system demonstrated to first year students by brave professors who prepare a small quantity of it, and after carefully drying it, cough or sneeze at it, thus setting up sound waves powerful enough to explode this erratic compound.

Even when tied to more domesticated elements than nitrogen, iodine finds bondage a nuisance. There is potassium iodide—a compound so stable under ideal conditions that it can stand without flinching temperatures up to 720 degrees C., where it will go off in a vapor, yet without decomposition. But if the union is sour—that is slightly acid—iodine sneaks to its freedom and the chemical friendship is soon off-color.

Perhaps such a vagabond trait may be a blessing in disguise—for most of the medicinal demands—if not the industrial demands upon iodine, call for it to exercise its properties as a free agent. For it is thus that it seems to operate best in the body cell.

LIFE THE CHEMIST

Yet even the most stable compounds acquire instability when Life must have their molecules. There are chemical changes constantly operating in our moist tissues, operating at low temperatures, and yet producing results that the chemist cannot duplicate under anything like the same conditions.

Consider the production of hydrochloric acid from salt, whereby our gastric utensils are kept to their acid constant. And so, it seems, that Life has a wizard chemistry all its own, and that we have still a lot to learn about its enzymatic, catalytic, electrolytic bag of tricks.

Thus do we humbly approach a consideration of the performances of iodine in the life processes of plant and animal.

Before so doing however, brief consideration will be given to the uses of iodine in the arts and industries, as well as to its uses as an antiseptic.

IODINE IN BUSINESS

Iodine *per se* has little use in the industries, although its compounds find practical application in many fields. A number of important dyestuffs contain it, and are possessed of unusual brilliance.

In photography silver iodide once had a wide use. It was the chemical chosen by Daguerre and Urepce in 1839, in their then startling process known as the "daguerrotype." A silver plate was treated with iodine vapors until a superficial layer of iodide of silver had been formed upon it. After exposure in a camera, the latent image reduced by light to elemental silver, was developed by treatment with mercury vapors which attacked the plate, forming silver amalgam in such places where the light had acted, while in the dark places they left the silver iodide surface unaltered.

LOOKING "DAGGUERS"

The picture was next fixed by washing with a solution of cyanide of potassium, which dissolved away the unaltered silver iodide. Think of the hazards involved in reproducing our grandmother's wedding party—when the poor photographer had to run through a gamut of poisons—from mercury to cyanide. No wonder some of the characters on old fashioned tin types look as if they too had tasted the cyanide.

Nowadays silver bromide is more commonly used in the emulsion, although many special plates and papers of silver iodide are still in use.

A very poisonous compound of iodine with cyanogen, is iodine cyanide. It has some use in taxidermy for preserving insects and butterflies.

The iodides of copper and mercury mixed with water, turn greenish black when they attain to temperatures over 200 degrees C. For this reason they are used to play policemen on rapidly running machinery bearings, to warn of an undue rise in temperature.

So too are they used in detecting the efficiency of sterilizers, autoclaves, etc.

Lead and cadmium iodide have a considerable use as a pigment in bronzing, in mosaic work, in photography.

IODINE—THE ANTISEPTIC

Elemental iodine has a distinct property which it does not always confer upon its compounds, except those which freely dissociate. It is the property of attacking germs. Of course, like most germicides, iodine does not always know how to differentiate between a good germ and a bad germ.

One of the facts so often overlooked in considering germicides is that they are inimical not only to germs but also to other forms of life. Carbolic acid kills the staphylococcus wintering in the carbuncle in the professor's neck—the same chemical will kill the owner of the carbuncle if it is applied inside his neck and not outside of it.

Bichloride of mercury is a fine germicidal agent, and an equally efficient suicidal agent. Arsenic is rough on rats—and just as rough and rough in the same way on the germs of syphilis—but arsenic, you may remember was the poisonous ingredient in Toffana water—that Saint-illumined beauty lotion, which when given internally—never failed in its sanctifying business.

And so it goes with most of our antiseptics and germicides—with the good they do in paralyzing the wicked germ—they interfere with normal living processes. It is a trite though often correct observation—that an operation may be successful though the patient pass on.

Equally correct is it to say that any vicious germ floating in the blood stream can be killed by introducing into the circulation the appropriate poison—only that the germ's host will be quite as abruptly killed.

The ideal germicide is the one that kills invading germs with the least possible damage to the living tissue harboring the germ.

Of course we must remember also, whether we like arithmetic or not, that the dilution factor always enters into the question of germicides. Einstein's theory of relativity may be hitched to the stars, but it touches most every earthly problem too.

So with germicides—so with poisons. The ideal germicide might be defined as one which is not poisonous to animal cells in doses fatal to disease germs—one which is chemically compatible with tissue, one which has a high coefficient of penetration and one which stays just long enough in the tissue to perform its germ-killing ministry. Efforts have been made and are constantly being made to gather together as many as possible of these conditions into the conduct of new antiseptic chemicals.

ANTISEPTIC PARTNERSHIPS

Thus in the new and colorful antiseptic mercurochrome, the highly toxic qualities of mercury and its poor rate of dispersion, due to local coagulation, are compensated for by fluorescein, a dyestuff of high penetration and low toxicity. By the way the latest manifestation of mercurochrome is in the new germ-proof, kiss-proof and soup-proof mercurochrome lip salve.

A similar combination of iodine with fluorescein is already available under the name of iodeosine (tetra-iodo-fluorescein $C_{20}H_8I_4O_5$). It has been used as an indicator, and possesses a color degree of dizzy red, not quite as spectacular however, as that of mercurochrome. So far as I know it has never been suggested as an antiseptic. It is unfortunately insoluble in water, although freely soluble in alcohol. A water-soluble sodium salt of this compound is known as erythrosine, and is a permissible coal tar color for camouflaging food. For all we know then, the bright red pop soda water of circus days may make a better gargle than a beverage.

THE MICROBE KILLER

Let us now consider the status of free iodine as a germicide. Elemental iodine has a phenol coefficient of 4, that is, it is four times as effective as carbolic acid in squelching bad microbes. A 1-1000 solution is sufficient to kill most vegetative forms of bacteria including the staphylococcus, tubercle and typhoid bacillus. Dr. Lambert, reporting in the *Journal of Experimental Medicine* in 1916, states that of all the germicides then tested on germs in the presence of living tissue, a weak solution of iodine was the only one which would kill the bacteria without injuring the tissue cells.

The Research Department of the Philadelphia College of Pharmacy and Science is now working with an isotonic solution of iodine which may to advantage replace the once famous Dakin's solution.

The commonest methods for exhibiting the medicinal as well as the germicidal effects of free iodine are in the form of alcoholic solutions such as the tinctures of iodine and in aqueous solutions, such as Lugol's, where potassium iodide is used to increase the solubility of the iodine.

Tincture of iodine is a 7 per cent. solution of iodine, with 5 per cent. of potassium iodide, in alcohol. The potassium iodide is added in order to permit the tincture to be diluted with water without pre-

cipitating the iodine, and also to render it less likely to form compounds with the alcohol.

As a household antiseptic tincture of iodine has no equal. It combines the therapeutic qualities of iodine, as a counter-irritant and germicide with the local values of the solvent alcohol. It has a high degree of penetration in spite of its theoretical incompatibility with tissue. It is still the surgeon's first choice in rendering sterile the site of operation. When that part of the anatomical landscape has been selected where the surgeon wishes to open his subject, the customary anteslicing performance is a generous dousing with an alcoholic or an ethereal soap solution. After a water wash this is followed by a liberal allowance of tincture of iodine. After a brief delay to permit the iodine to execute every single germ on location, the stain is cleared with alcohol, and the surgeon now gleefully goes to work. That is how much confidence most surgeons have in tincture of iodine.

THE SURGEON'S CHOICE

As a local antiseptic application to fresh wounds and bruises—as a mild counter-irritant, it is not likely that any of the new dye compounds are superior to the century-old alcoholic tincture of iodine. Of course it has some disadvantages—as have all blessings. Its dark disagreement with starched garments, its tendency to concentrate on long standing in unstoppered vials, its bad behavior when too tightly bandaged, and its poisonous nature when taken internally, are all against it.

Yet its stains with starch are readily removed with photographic hypo (sodium thiosulphate). Its tendency to concentrate on long standing in unstoppered vials is easily avoided by keeping it in stoppered vials, and not too long. Its bad behavior when a sore bathed with it is too tightly bandaged can be similarly avoided by withholding the bandage.

So too can its suicidal charms be minimized. As a matter of fact one who chooses tincture of iodine as an easy means to an end, is unesthetic and unreasonable and indelicate, particularly if the last meal was tapioca or rice pudding. As a suicidal implement drowning is quicker, cheaper and cleaner—whereas tincture of iodine is uncompromisingly slow and painful.

But to return to the sensible uses of iodine.

For convenience sake tincture of iodine or other forms of iodine are supplied to the laity in special applicators, such for instance as

the iodabs, and the iodamps. Iodabs are short sticks tipped with dry colloidal iodine and intended for local application, after having been first moistened with water.

AN IDEA! Before dismissing the subject of iodine for local application, it has occurred to the writer that the standard book of medicine (the Pharmacopœia) would do well to include a weaker preparation of iodine for domestic use, such a preparation to contain 2 or 3 per cent. of iodine in a mixture of equal parts of alcohol, glycerin and water.

The U. S. P. H. S. has advocated the use by campers and others, of tincture of iodine as a convenient means of sterilizing drinking water. Two drops to a glassful of water, upon five minutes contact, will efficiently sterilize it, and leave no unpleasant taste.

It is the writer's belief that the old fashioned gargle made by adding a teaspoonful of salt, a teaspoonful of vinegar and a teaspoonful of tincture of iodine to a pint of water is still without equal.

Compounds of iodine too, are quite popular as an antiseptic.

"I know a bank where the wild thyme grows"—that oft recurring mechanism which youngsters are sentenced to parse in their grammar classes is only an antiseptic utterance, for wild thyme is now known to contain a germ-killing compound called thymol—which when linked to iodine forms that popular dusting powder known as thymol iodide.

Just beyond the bank where the wild thyme grows is a marsh where as children we used to watch the queer bubbles rise out of the mud, and which we exploded by touching with a match. Now that is marsh gas or methane. Linked to chlorine in a certain proportion this gas produces chloroform, and in another proportion carbon-tetrachloride, the far-famed fire fighter.

But linked to iodine, marsh gas becomes the jaundiced, foul-smelling iodoform. Of course there are many other ways of producing iodoform such for instance as the union of alcohol, alkali and iodine. Now iodoform, commonly called "the hospital smell," is a splendid antiseptic dressing, and only its bad odor prevents its wider use.

A practical joker in medicine has developed a so-called odorless iodoform, which in reality is nothing more than iodoform mixed with a vanilla like chemical (coumarin), purposed to mask the iodoform odor. Silver iodide in colloidal suspension is also used as a valuable antiseptic.

There are many other medically used compounds of iodine, too numerous to mention.

THE "INSIDE STORY" OF IODINE

The internal uses of iodine and its compounds are not for our consideration here, sufficient for us to state in passing, with reference to iodine, that at some time or another, some compound or another has been used in some plan or another, in the treatment of some form or another of every disease ever known to have oppressed humanity.

In internal medicine such a statement as this is not an exaggeri*sm,* no matter what drug it described. That is the custom—that is the system. Unbelievers in the audience are referred to older issues of the U. S. Dispensatory, where they may find many such panegyrics on the proclivities of unparalleled panaceas, now hardly ever in use.

Iodine when brought in contact with certain vegetable oils, will in time unite with the fatty acid molecule in a very definite way. Its quantitative union with such oils is now used as a factor to determine their identity and purity. Such iodine-oil products are also used as a means of administering iodine internally, their alleged advantage being a slow but steady and thorough iodine liberation and medication.

In addition they have been used as injections in X-ray practice to delineate tissues which when not so injected, do not project their shadow on the plate. Lung pictures and kidney pictures are so taken. A compound of iodine with phenolphthalein (tetraiodophenolphthalein) when injected into the blood will travel unceremoniously through the system until it reaches the gall bladder, where it will sit down to rest its molecules.

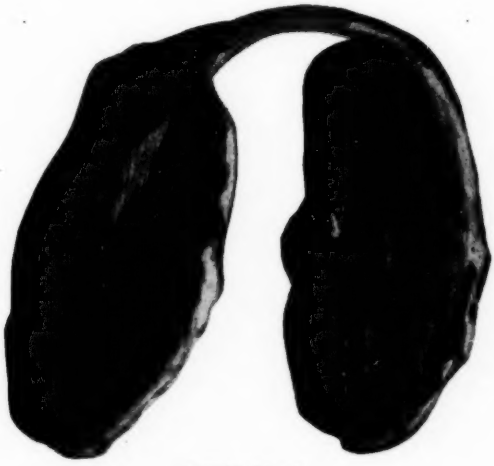
IODINE GOES VISITING

If an X-ray picture be taken of the gall bladder under normal conditions, very little if any of its detail may be seen. If, however, a picture be taken while this iodine compound is visiting, the whole outline of that organ may be clearly seen as well as any imperfections it may have.

And here, at last, we approach the interesting part which a very small quantity of iodine plays in our every performance—and to a great degree makes us whatever we are.

YOU AND I!

In 1895 E. Baumann, a German physician, discovered that iodine was one of the important, if not the most important, elemental constituent of the thyroid gland. This gland consists of two maroon colored masses located astride the gastronomic chute above the windpipe, and close to the larynx. Connecting the two lobes which are about two inches long and less than an inch in width, is a narrow isthmus of the same tissue. These lobes appear very much like the flaps of an open purse. The only portion of the normal gland that is readily palpable is this isthmus which



Thyroid Gland.

is attached to the trachea, and may be felt riding under the finger during the act of swallowing.

Because of the tendency of this gland to become enlarged and to constitute the prominent deformity known as goiter, it has always attracted a great deal of attention. Normally in man this gland weighs less than an ounce (20-25 gm.), or about 1-2000 or 1-2500 of body weight. This ratio however, is exceeded in infants and in women.

The purpose of the thyroid gland in the body organization seems to be to control the speed of living, in the chemical sense. Physiologists call this a regulation of the metabolic rate. This it does in some mysterious way by keeping constant the iodine content of our blood stream.

THE SPEED OF LIVING

Thus a thyroid gland which is over-producing accelerates every body function—over-activates the fires wherewith our food, and flesh are burnt away—overworks our thinking mechanism—over-sensitizes our nervous system—over-circulates our blood—and overwhelms our muscles. And everything we do we over-do—and death comes that much sooner.

Thyroid and Parathyroid Glands in Human Throat; the the two small parathyroid glands are imbedded in either thyroid lobe. After Halsted and Evans.

And a thyroid gland which is under-producing slows up the system—under activates the fires wherewith our food and flesh are burnt away, so that the system accumulates poisons—underworks our thinking mechanism—we become dull and drowsy—undermines our nerves and muscles—and we grow awkward and clumsy—underfeeds the blood and so invites infection. Everything we do we under do—and death comes that much sooner.

Thus in so relatively small a matter as iodine and thyroid functioning—we are impressed with the chemical delicacy of adjustment within us, which makes us the trivial toys of a mite of iodine.

But the remarkable thing today is that with the intelligent use of the thyroid gland from our less fortunate animal brothers and sisters—such as the ox and the sheep, or with the chemical equivalent of the gland in the form of thyroxin and other iodine compounds—many diseases due to thyroid abnormalities may be prevented or even cured.

The metabolic rate of an individual can now be easily studied—and treatment given accordingly.

But as with all such medical discoveries—quacks soon came to abuse them.

GIRTH CONTROL

Listen to the poet—

"Some grow fat with faulty fare,
And some grow fat with laughter."

Now rotundity might have been fashionable once upon a time—but not in these reducing days. Cosmetically and costumically—the fashion of the day calls for the shortest line between two parallel perpendiculars, and mathematically the frail sex has determined upon being reduced to the least common denominator.

The quack soon saw the trick of thyroid and capitalized it. For with its administration to a normal person under lessened diet the body fires burn more brightly—and flesh is broiled away. Surely it will cause a reduction of weight—but it so disturbs other body processes that its use may bring not only a reduction in avoirdupois, but a definite reduction in one's lease on life. Thyroid should not be self administered except under competent medical supervision.

Another recent claim is that baldness is due to a thyroid deficiency. Naturally there were those who at once turned to thyroid medication for cranial reforestation. But again the hazards are too great.

Chatin in 1852 pointed out that goiter was more common in those regions where the soil and water were very low in iodine. Other diseases such as myxedema, and exophthalmic goiter (Grave's disease), were later associated with the thyroid and with iodine.

Cretinism, that dreadful disease of infancy, a disease which once afflicted whole communities is due to a congenital thyroid deficiency. Certain parts of Switzerland, prior to the past quarter century, regu-

larly turned out their quota of cretins. Thirty years ago the cretin was looked upon as a hopeless idiot. Brought into the world as a monstrosity, he failed to develop mentally and physically—and always remained a helpless burden to society. Today by prophylaxis and by treatment, the output of cretins is being annually reduced.

So, too, is the incidence of goiter in spite of its former geographic discrimination. And all of this because the role of iodine in biologic processes is becoming better understood.

THE THYROID IODINE FACTORY

The thyroid gland is present in all vertebrate animals beginning low down in the scale, with the lampreys and complicating its structure and increasing its size as it occurs farther up in the evolutionary scale. In fish the thyroid occurs as small scrubby patches little larger than pin heads—scattered along the important blood vessels. Then in the reptiles it is a little larger and more compact, and still more prominent among the birds and the mammalia. But it is in the primates and in man that it attains to greatest size. Thus it might be said that the thyroid gland is an indicator of evolution.

The farther we are from our early home in the sea the larger the thyroid gland. Now if evolution continues along the same line—a million years from now our thyroid may have become the most important organ in our bodies. And man's appearance may be consequently so changed that instead of being the good-looking creature he thinks he now is—he will have evolved into a pop-eyed, fat-headed, chinless creature—the space between his chin and his collar button having been taken over by his constantly expanding iodine plant.

But that is too far off to worry about. Several things may happen in a million years.

CUM GRANO SALIS

Certain authorities claim that all life was once marine or submarine—that the antecedents of every creature now living, originally like Venus, came from the sea. How they came to own this information is more than I can tell—but that is their story. Just where the sea secured its life is a question they have not ventured to answer.

One of the slender threads wherewith they join their arguments is in the remarkable comparison which they make between animal blood and sea water. When blood is permitted to coagulate the clear, rather colorless serum or plasma which separates, has, exclusive of its protein content, a composition very like that of sea

water. It contains so much sodium chloride—so much phosphates—and carbonates—and so much combined iodine—in a ratio similar to that of sea water.

The contention is that whereas we were once limpid jellyfish that floated lazily on the dark primeval seas—we are now so evolved and involved that a share of the sea floats diligently within us, with an ebb and flow in every heart beat.

Certain we are that life in us could not get along without the sea elements that race in our blood stream. Lacking the little salt that parades its molecules constantly—through sleep and waking periods in us—no longer would life reside—nor indeed would life stay with us without our mite of iodine.

And what a mite it is. Listen. The high tide of iodine in the blood is about one grain of iodine to ten million grains of blood, or less than a hundredth of a grain to the entire circulation. The reservoir of iodine in the body, namely the thyroid gland, only holds a third of a grain (about 25 milligrams) and in order to keep this reservoir full one only has to consume per day, in his food or drink, less than a thousandth of a grain of iodine. No wonder some folks believe in homœopathy. It seems the Great Designer did!

IODINE DAY ON FRIDAY

I do not know the canons of the Church of Rome nor its history, well enough to identify the origin of the custom of sea-food for Friday. In any event it is a good custom, for though Friday euphoniously admits of a fry—fried fish will furnish our weekly requirements of iodine far better than anything else we might fry, or try. And so, much like the Mosaic indictment of pork† whereby our Jewish friends are denied the gastronomic joys of a ripe red ham (unless they call it pickled salmon) the Friday fish day may have had a dietary hygienic value.

I mentioned 1895 as the year of the discovery of iodine in the thyroid gland. The form in which iodine is present in the gland was reported by the American Kendall as late as 1916, and named by him Thyroxine. It is a crystalline compound containing 65 per cent. of iodine. In 1926 Harrington of London more accurately described it, and in 1927 duplicated it by synthesis, in his chemical laboratory. So that you may have some idea of the complexity of

†Hog meat particularly in the Orient and near-Orient harbors a parasite which can infest and infect the human system (Trichinosis) producing a vicious disease. Moses was not a bacteriologist, but he had a fine understanding of sanitation and public health measures.

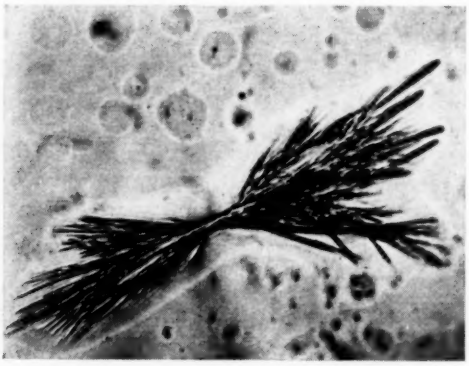
Harrington's duplicating job, here is the full chemical Christian name of the substance: beta-tetra-iodo (3, 5, 3^1, 5^1)-4-(4^1-hydroxy-phenoxy)-phenyl-alpha-amino-propionic acid.

So it seems evident to us that intimate knowledge of the role of iodine in life is quite modern.

But listen, while London was yet a muddy fen and Rome a rambling village—China had a mind of her own—and a culture of her own. When the civilizations of Athens and Rome were yet in knee pants—Cathay had spun her cycles.

CHINA KNEW

Four thousand years ago the Chinese had guessed that goiter was a disease related to diet—that it mostly attacked people who lived away from the sea—that it yielded sometimes to treatment with sea medicaments—salt of the sea—sponge from the sea—sea-weeds and coral. Yes, indeed, the art of the ancients was in knowing how—not why.



Thyroxin-Crystal of Kendall's own preparation.

Later Dioscorides, a Greek physician, and author of a treatise on Materia Medica, recommends the use of sponge to "check tumors"—and if we assume that by tumors he meant goiters, we have to admit that he "knew his sponges." The Syriac Book of Medicines (200-300 A. D.) directs "burn a sponge in the fire, crush it in wine and administer as a draught."

And so was burnt sponge used in medicine for centuries, only to be displaced in modern times by iodine and its compounds.

Indeed the first Pharmacopœia of the United States, published in Boston in 1820, gave it a place though it was deleted in the next revision. So too was a variety of burnt sea weed included.

Today burnt sponge and bladder-wrack are still used by the eclectic physicians, who believe that these natural products in contradistinction to iodine or its definite artificial compounds, contain a structural "something" that must be very different from pure iodine or a single iodine compound. And they may be right.

SPONGE

A strange fact regarding sponge is its property while alive of abstracting iodine from sea water. In some tropical species of sponge the iodine content of sponge ash may run as high as 8 to 14 per cent.. while seaweed ash from which some commercial iodine is obtained rarely exceeds 1.5 per cent. Since it is assumed that all the iodine in sponge comes from sea water and sea organisms, it has been calculated that one pound of sponge contains the total iodine content of twenty thousand tons of sea water. Rather a remarkable figure.

Most all sea organisms, plants and animals too are rich in iodine. As previously mentioned much of the iodine of commerce is obtained from such sources. Even the humble oyster, whether brought up in well-aired beds or not, contains his share of iodine.

Sea water contains about 1-300th of a grain of iodine to each gallon (0.05 mgm. per Liter.). It is of interest in passing to note that the Great Salt Lake of Utah contains but a little more iodine (about 1-200th grain to the gallon), whereas it contains five times as much salt.

Of interest too is the fact that we have enough iodine in the sea to last our children for a long, long time. Practically all of the iodine in this planet is in the sea and a dabbler in useless arithmetic has figured that it amounts to a few pounds short of sixty billion metric tons, which antiseptically leaves us nothing to worry about.

Plants and animals which now reside in the sea are not alone in their iodine content. For land plants, too, in varying amounts, contain this element. The sugar beet, for instance, contains more than a trace of it, and recently special fertilizers containing small amounts of iodine have been recommended for this vegetable. Watercress too, contains considerable iodine, and so do many other plants.

IODINE—LANDSMAN

It is assumed, however, that the presence of iodine in plants and in the lower forms of animal life may be incidental to its presence in the soil, and in certain inland waters. In rock formations iodine is frequently asso-

ciated with the minerals, particularly copper, silver and mercury. Soil and sod, too, contain its compounds, though in very small and variable amounts. The volatility of the element suggests its presence in small amounts in the atmosphere, too. Generally speaking the soil of coastal regions is higher in iodine content than that of inland regions.

It has been a well-intentioned assumption that iodine, like its cousin chlorine, is wafted inland in the form of spray from the halogen rich oceans, and that these elements are thus literally sprayed over the land, finding their way to soil and sod and running waters. And this of course, explains why iodine hugs the coast line.

As with most assumptions of this nature, the truth is only partially met. However, it has been recently pointed out that while the salt spray theory of iodine distribution seems to have gained general acceptance, the Atlantic Ocean contains only twenty-three parts per billion of iodine, and *five or six parts per billion* in the water of streams cannot come solely from spray unless the waters contain a like proportion of the other salts of the sea, which they do not. As for foods grown on land, in South Carolina there is a tendency to higher iodine content in that part of the state which is more distant from the coast and nearer the Blue Ridge of the Appalachian Mountains. It has been suggested, therefore, that the main source of iodine in the vegetation of such regions lies in the disintegration of the granite rocks, and that this has been supplemented by the liberal use of commercial fertilizers over a period of years. This supply of iodine is being conserved by the return of vegetable matter and animal wastes to the soil.

CAROLINA MOON

South Carolina has capitalized the alleged heavy iodine content of her vegetables by ridiculously adding the word IODINE to her automobile license plates, and by circulating a silly slogan—

A potato a day
Keeps goiter away.

Which shows how the low surface tension of ignorance can make even the so-called authorities run away from sound sense. The "Carolina Moon" *will out.*

Yet much has been constructively done to awaken the world to the realization of the fact that iodine deficiency in food is the commonest cause of goiter and other diseases. The resulting world-wide movement to insure the presence of sufficient iodine in the diet to prevent these dreaded diseases is one of the greatest prevention measures undertaken by man in the interest of good health. Yet the wholesale methods used have not been without danger for there are types of gland affections which are radically aggravated by iodine medication, and are only amenable to surgical care.

IODOPHOBIA

Had we more time at our command we might have dwelt more fully upon these prophylactic measures —such for instance as the now tabooed charging of drinking water with iodides, or the general use of iodized salt. Iodized salt, containing from 0.02 to 0.025 per cent. of iodine in the form of iodides, is now available in the stores. But we repeat that with community medication of this kind it must not be overlooked that harm can come from feeding iodine to individuals who already have enough or too much, just for the sake of catching those who have too little. It is a matter always of individual treatment. Nor must we overlook the danger of inducing in the individual through over-dosage that uncomfortable chemical disease, iodism. Indeed it is not always a matter of over-dosage for to iodine as well as to most everything there are persons who display idiosyncrasy.

Then too, we might have discussed the role which the thyroid and other glands played in the differentiation of the human family, insofar as color and race are concerned—for once, so it is said, all men were black. The change in our pigment, in our physique and physiology has been largely due to the refined alchemy of those little internal laboratories which we call glands.

Theirs is the verdict of our personality. They are the architects of our qualities and the arbiters of our destinies. If ever man shall know just how human nature may through their use be bettered—or be controlled—then he will have reached Utopia.

THE NON-VOLATILE CONSTITUENTS OF MENTHA PIPERITA

By Herbert Adolph Braun*

THE HISTORY of the peppermint plant previous to 1696, the year in which John Ray collected, in Hertfordshire, the herbarium specimens still preserved in the British Museum, is more or less dubious. Gaubius, in 1771, makes mention of the substance he designates *Camphora europaea menthæ piperitidis,* our menthol.[1] Since then the volatile oil of peppermint has been examined repeatedly by chemists, but our knowledge of the volatile constituents of the plant is based primarily on the thorough investigation of Power and Kleber [2] of 1894. The second edition of Gildemeister [3] enumerates no less than seventeen definite chemical compounds. The water-soluble constituents have been investigated by E. R. Miller,[4] R. E. Kremers [5] and G. H. Gordon,[6] who have isolated no less than ten different constituents from the cohobated liquors.

Peppermint has been cultivated on a large scale since the middle of the 18th century,[7] however, almost exclusively for the production of its volatile oil. It is, no doubt, because of this that, whereas we know of twenty-nine different volatile constituents of this plant, we know next to nothing of its non-volatile constituents. Thus, Wehmer,[8] in his phytochemical Beilstein, makes mention only of inorganic constituents and indicates the presence of tannin. That cellulose and other carbohydrates, also chlorophyll occur in the plant is generally accepted even if not specially proven.

In order to acquire a better knowledge of the biochemistry of a plant, it is necessary to study it from all angles, not merely from that *e. g.* of its volatile compounds, all of which, in this instance, constitute

*Fritzsche Brothers Fellow.

[1] Gildemeister und Hoffmann, *Die aetherischen Oele* (2d ed.), vol. I, p. 205.

[2] *Pharm. Rundsch.*, 12, p. 157.

[3] Gildemeister und Hoffman, *Die aeth. Oele* (2d ed.), vol. III, p. 526.

[4] *Wis. Pharm. Exp. Stat. Circ.*, No. 7 (1919).

[5] *Ibid.*, No. 11 (1920), p. 10.

[6] *Amer. Journ. Pharm.*, 99 (1927), p. 529.

[7] Gildemeister und Hoffman, *Die aeth. Oele* (2d ed.) vol. I, p. 204.

[8] Wehmer, *Die Pflanzenstoffe,* p. 662.

but a small percentage of its chemical components other than water.[9] So far as the Labiates are concerned, a good beginning has been made by S. M. Gordon in "The Non-volatile Constituents of *Mentha aquatica.*" [10] Similar studies of Monarda species are well under way in this laboratory.

Inasmuch as this chemical examination of the leaves of *Mentha piperita* parallels that by Gordon of *Mentha aquatica,* the results of the two studies will be compared at the close of the report on the experimental investigation. With this comparison another step in the study of the "Biochemistry of the Mints" [11] has been taken. True, it is only a first step, but it may be regarded as a step in the right direction for the results afford a better, though by no means a complete picture of the life processes of these plants.

Experimental Part

Source of Material. Some 36 lbs. of peppermint leaves, harvested in the Pharmaceutical Garden during the summer of 1926, were subjected to a preliminary chemical examination during the

[9] The percentages herewith tabulated apply to the leaves only, not to the entire plant.

Moisture removed by air drying	85.2 p. c.
Moisture content of air dried leaves	6.2 " "
Total water content	91.4 " "
Other constituents (by difference)	8.6 " "
	100.0 " "

Computed with reference to the other than water constituents of the leaves the percentages are herewith tabulated:

	For fresh leaves	For leaves minus water
Volatile oil	0.04 p. c.	0.46 p. c.
Other volatile material	Traces	Traces
Non-volatile extractive	4.54 p. c.	52.79 p. c.
Non-extractive (cellulose, etc.)	4.02 " "	46.75 " "
Total	8.60 " "	100.00 " "

As stated, the "other constituents" were computed, not actually determined, because of the unsatisfactoriness of extractive, etc., determinations. The computations to the second decimal are recorded, not to make a show of accuracy that is not attainable, but because the yield of volatile oil is so small that it had to be recorded in the second decimal. Hence, in order to make the total percentage an even one hundred, the percentages of non-volatile extractive and non-extractive had to be computed to the second decimal.

[10] *Am. Journ. Pharm.,* 100 (1928), pp. 433 and 509.

[11] *Journ. Biol. Chem.,* 50 (1922), p. 31.

academic year 1926-27. No separate report of this work will be rendered, but certain results may be reported in connection with the work here recorded.

From August 11th to 13th, 1927, a larger amount of peppermint, cultivated in the Pharmaceutical Garden under the direction of Professor W. O. Richtmann, was collected and dried. Owing to the dry season, the plants had not arrived at full bloom. The leaves, separated from the stems, weighed 159 lbs. (= 57 p. c.) whereas the stems weighed 119 lbs. (= 43 p. c.)

Moisture Determination of Leaves. Five g. of comminuted leaves, when distilled with xylene [1] yielded 1.56 cc. and 1.54 cc. respectively of water, corresponding to 6.24 and 6.16 p. c. of moisture.

Ash Determination of Leaves. I. 0.8070 g. yielded 0.0412 g. of water-insol. ash and 0.0536 g. of total ash.

II. 0.6153 g. yielded 0.0313 g. of water-insol. ash and 0.0580 g. of total ash.

The percentages are herewith tabulated:

	I	*II*
Total ash	6.64 p. c.	6.89 p. c.
Water-insol. ash	5.11 " "	5.08 " "
Water-sol. ash	1.53 " "	1.81 " "

Pentosan Determination of Leaves. The phloroglucinol method [2] was followed and 5 g. of material were employed for each determination. For the computation of the pentosan the following formula was used $(a + 0.0052) \times 0.8824$; for the computation of the pentose the formula $(a + 0.0052) \times 1.0026$.

	Wt. of phloroglucide obtained	Pentosan Weight	Pentosan Percentage	Pentose Weight	Pentose Percentage
(1)	0.3490 g.	0.3125 g.	6.25 p. c.	0.3551 g.	7.10 p. c.
(2)	0.3522 "	0.3153 "	6.31 " "	0.3558 "	7.16 " "

Quantitative Extraction of Leaves with Selective Solvents. Inasmuch as the extractions according to Dragendorff were conducted

[1] *Circular 134, Forest Service, U. S. Dept. of Agr.*
[2] *Handb. of Agr. Chem.*, p. 96.

with a 100 g. sample, the results recorded in grams correspond to percentages as well.

	No. of Gms. of Extract
Petroleum ether	2.6 g.
Ether	2.2 "
Chloroform	4.3 "
Ethyl alcohol	12.5 "
Water (cold)	32.1 "
Water (hot)	6.2 "
10 p. c. HCl-	17.1 "
10 p. c. NaOH	14.0 "

Ash Determination of Stems. I. 0.8146 g. yielded 0.0767 g. of water-insoluble ash and 0.1259 g. of total ash.

II. 0.5180 g. yielded 0.1374 g. of water-insoluble ash and 0.2309 g. of total ash.

	I	*II*
Total ash	15.46 p. c.	15.21 p. c.
Water-insoluble ash	9.42 " "	9.05 " "
Water-sol. ash	6.04 " "	6.16 " "

Extraction. One hundred pounds of comminuted dry leaves were extracted with 95 p. c. alcohol in a Lloyd Extractor, 25 lbs. being used as a charge. From the results herewith tabulated, it becomes apparent that the first two batches were not completely exhausted.

Batch	*Length of extraction*	*Amt. of semi-solid extract*
No. 1	3 days	2.26 kg.
" 2	3 "	2.64 "
" 3	7 "	3.69 "
" 4	6 "	3.28 "
		11.87 kg. corresponding.

to 26.16 p. c. of the dried leaves. The volatile constituents were removed by steam distillation, 101 g. of volatile oil resulting. This corresponds to 0.85 p. c. of the concentrated alcoholic extract, or to 0.19 p. c. of the dried leaves.

After steam distillation, the non-volatile extract separated into two layers:

A. An upper, oily or resinous sticky mass with an acid reaction. This was thoroughly washed with warm water and the washings were added to B.

B. A lower aqueous solution. Having been shaken with petroleum ether and then with ether it was evaporated to soft extract consistency when it weighed 6.59 kg., hence represented 54.67 p. c. of the original alcoholic extract.

The black, resinous mass remaining after the removal of the volatile oil and of the water-soluble extractive from the alcoholic extract, was shaken with petroleum ether, the hydrocarbon solution separated, and the solvent recovered. A black, viscid mass remained weighing 3.579 kg. corresponding to 30 p. c. of the water-insoluble alcoholic extract. The residual extract, after removal of the petroleum ether-soluble constituents, was shaken with ether, the ethereal solution separated and the solvent recovered. The ethereal extract thus obtained weighed 81 g., corresponding to 0.68 p. c. of the water-insoluble alcoholic extract. This treatment yielded three products:

1. A petroleum ether extract (fatty oil).
2. An ether extract (resin).
3. A residue insoluble in petroleum ether and ether.

Volatile Oil. 133 g. of volatile oil had been obtained from the 1927-1928 crop. This was of a dark green color. The oil was redistilled with steam whereby an amber-colored product weighing 78 g. was obtained. The 1926-1927 crop, however, yielded an oil which had a specific gravity of 0.8799 at 24° C. The optical rotation was –8.22° at 22° C. These constants are rather low, which fact may be attributed to traces of petroleum ether. This solvent was used by S. M. Gordon, who began the work on this problem, to shake out the fatty and volatile oils from the alcoholic extractive.

Fatty Oil. The impure fatty oil obtained as previously indicated was heated for two hours with 900 g. of potassium hydroxide dissolved in a liter of water. On cooling, a semi-solid soap rose to the surface which was removed by straining.

The semi-solid soap was dissolved in water and the aqueous solution shaken with ether until this solvent was no longer colored. The ethereal solution was dried with anhydrous Na_2SO_4. Upon recovery

of the ether, a residue weighing 277 g., representing 7.74 p. c. of the petroleum ether extract was obtained. (See Nonsaponifiable Matter.)

After extraction with ether, the lye was acidulated with hydrochloric acid and the acid liquid distilled. No volatile acids were isolated from the distillate.

Preparation of the Lead Soaps of the Fatty Acids. The potassium soap of the fatty acids which had been obtained by the saponification of the petroleum ether extract and from which the unsaponifiable matter had been removed by extraction with ether, was heated on a water bath to rid it of any retained solvent. After removal of the ether and after neutralization of any excess KOH with 1 : 1 HCl, a hot 10 p. c. lead acetate solution was added. A heavy, sticky precipitate consisting of the Pb soap, which was yellowish-green, was formed. It was separated by means of a suction filter and dried, first with the aid of filter paper and then by placing on a radiator. The yield of lead soap was 502 g.

Separation of the Saturated and Unsaturated Acids by the Lead Soap-Ether Method. The dried soap was refluxed for two hours with a large amount of ether which dissolved the major portion. The mixture was allowed to stand for about an hour when the ether was filtered off. More ether was added to the residue and the process was repeated until no more of the lead salt went into solution.

Unsaturated Fatty Acids. To the ethereal solution containing the soluble lead salts a 1 : 1 HCl solution was added. The $PbCl_2$ thus formed was separated by filtration. The ethereal layer containing the free unsaturated fatty acids was separated from the aqueous layer. Having been washed several times with water, the ethereal layer was dried over anhydrous Na_2SO_4. The ether was distilled off for the most part and the rest was allowed to evaporate spontaneously. 210 g. of a semi-solid residue resulted.

Bromination of the Unsaturated Fatty Acids. The liquid unsaturated fatty acids were dissolved in 10x their weight of glacial acetic acid and 2x their weight of ether. To this solution, after cooling in ice water, was added a mixture of equal parts of bromine and glacial acetic acid until there was an excess of bromine. It was allowed to stand in the ice box for 24 hours.

Separation of Linolenic Hexabromide. After twenty-four hours a precipitate had formed which amounted to 6.1 g. or 2.93 p. c. of the unsaturated fatty acids. It melted at 180-181° and was, therefore,

identified as linolenic acid hexabromide. A bromine determination, made according to the Stepinow method,[1] gave the following results:

0.1388 g. yielded 0.2078 g. of AgBr.	
Calcul. for $C_{18}H_{30}O_2Br_6$	63.27 p. c.
Found	63.71 p. c.

The ethereal solution from which the linolenic acid hexabromide had been separated was poured into a large volume of water. A brownish precipitate was formed which was for the most part soluble in petroleum ether. On standing in the ice box over night no precipitate was formed, showing an absence of linolic acid tetrabromide.

Isolation of Oleic Dibromide. Upon evaporation of the petroleum ether a small amount, viz. 2.72 ., of a brown oily liquid remained. This represents 1.29 p. c. of the entire fatty acid (unsaturated) residue.

A bromine determination, according to the Stepinow method, gave the following results:

0.2169 g. gave 0.2845 g. of AgBr.	
Cal. for $C_{18}H_{34}O_2Br_2$	36.18 p. c.
Found	36.27 p. c.

The fatty acid, therefore, may be regarded as oleic acid. It becomes apparent that only a small part of the unsaturated acids was isolated as bromides.

The Saturated Fatty Acids. A solid mass remained in the flask after the ethereal solution of the lead salts of the unsaturated fatty acids had been removed. Ether was added to the residue and then a 1:1 HCl solution in order that the Pb salts might be decomposed. The $PbCl_2$ resulting was removed by filtration. The acid aqueous layer was separated from the ethereal layer and the latter was repeatedly washed with water. It was then dried over anhydrous Na_2SO_4. The ether was partially distilled off, the rest being allowed to evaporate spontaneously. 102 g. of residue, which was of a deep green color, resulted.

An attempt to effect a separation of the solid fatty acids by means of their methyl esters was unsuccessful. Hence the acids were again liberated from their methyl derivatives.

[1] *B.*, 39 (1906), p. 4056.

Fractional Crystallization of the Fatty Acids. The fatty acids thus recovered had a green color. This was removed by refluxing with petroleum ether until all the fatty acids had gone into solution. A resinous substance remained behind. It weighed 42 g., making up 41.18 p. c. of the saturated fatty acid residue. 27 g. of saturated fatty acids which had only a faint greenish tinge were thus obtained by evaporation of the petroleum ether.

Fractional crystallization from alcohol was resorted to whereby the following fractions were obtained after repeated recrystallization:

		M. P.	*Quantity*
Fract.	I	59–59.5°	13 g.
	II	60–61°	5 "
	III	59–61.5°	2 "
	IV	84°	1.5 "
	V	96–97	2 "

Fractions I, II and III were bulked because of the similarity of their melting points. To the alcoholic solution an aqueous solution of barium acetate was added in order that the barium soaps might be obtained. In this procedure three fractions resulted: the first weighed 10 g., the second 4.5 g., and the third 1.2 g. Further addition of barium acetate failed to precipitate anything more.

Each fraction was saponified separately and, upon repeated recrystallization from alcohol, the mixed free acids yielded four fractions with the following properties:

	M. P.	*Amt.*	*Neutr. Val.*
a.	59–60.5°	0.5 g.	257
b.	60–61.5°	8.2 "	251
c.	57–57.5°	0.85 "	272
d.	57–58°	1.1 "	277

Fractions a and b had melting points and neutralization values corresponding closely to those of palmitic acid, while c and d are very likely mixtures of palamitic and stearic acids.

Isolation of Mellisic Acid. Fraction IV which had a melting point of 84° was repeatedly recrystallized from glacial acetic acid whereby the melting point was raised to 86°. The final yield was 0.61 g. A mixed melting point determination with pure mellisic acid (obtained from beeswax by S. Y. Chen), revealed no depression.

A silver salt was prepared which on ignition gave the following results:

0.1321 g. of Ag salt yielded	0.0251 g. of Ag
Calculated for mellisic acid	19.28 p. c.
Found	19.05 p. c.

The acid, therefore, corresponds in its composition to mellisic acid.

Separation of an Acid $C_{18}H_{36}O_2$. The last fraction (V) was recrystallized from glacial acetic acid a number of times whereby a small amount, about 0.12 g., of a fatty acid was obtained. This had a melting point of 100–101°. A silver salt was prepared which on ignition, gave the following results:

0.0067 g. of Ag salt yielded 0.0018 g. of Ag.
Percentage of Ag calculated for $C_{18}H_{35}O_2Ag$ = 27.56 p. c.
" " Ag found in compound = 26.96 p. c.

This result, however, should be confirmed since the amount of the fatty acid available was too small to run a check on the silver determination. No acid of the formula $C_{17}H_{35}COOH$ with a m. p. of 100–101° is recorded in the literature.

Isolation of Glycerol. After separation of the fatty acids from the saponification liquid, the aqueous acid solution was neutralized, decolorized with bone charcoal and evaporated. The recrystallized salt was removed from time to time. The residue gave a test for acrolein when heated with $KHSO_4$. Acrolein was identified not only by its odor, but by reducing an ammoniacal solution of $AgNO_3$, also by giving a blue color with sodium nitroprusside and piperidine.[1]

Examination of the Unsaponifiable Matter. 277 g. of unsaponifiable matter, representing 7.74 p. c. of the total petroleum ether extract, were obtained. It was a semi-solid, orange-colored material. The entire residue was dissolved in one liter of alcohol and the solution allowed to crystallize.

Separation of a Hydrocarbon. After standing a few days 9.6 g. of a substance separated out. On repeated crystallization from ethyl acetate, it melted 69–69.5°. Attempts to make an acetyl or a benzoyl derivative failed for the substance retained its melting point of 69°

[1] Rosenthaler, *Grundzüge der chemischen Pflanzenuntersuchung*, p. 49.

after benzoylation and acetylation, so that it became evident that this was not a wax alcohol but probably a hydrocarbon. A hydrocarbon, $C_{31}H_{64}$, hentriacontane, is recorded in the literature as having this melting point.

Separation of Phytosterol. On further evaporation of the alcoholic solution four fractions of crystals resulted which had the following melting points:

Fraction	I	125°	0.3 g.
"	II	126°	0.71 "
"	III	128°	0.84 "
"	IV	132°	1.1 "
			2.95 "

Further attempts to obtain more fractions failed.

Because of their similarity of melting point these fractions were combined and after repeated refractionation from alcohol a substance having a melting point of 134–135° was obtained. This substance gave the color reactions of phytosterol. A portion of the phystoterol was treated with acetic anhydride when an acetyl derivative was obtained.

The latter, when crystallized from warm alcohol, separated in fine colorless needles melting at 123° which corresponds to the m. p. of the phytosterol acetate found in literature.

Residue. After removal of the hydrocarbon and of the phytosterol no further crystalline substances separated. The residue was a thick orange oily liquid and very likely consisted of yellow pigments related to chlorophyll, namely carotin and xanthophyll. It amounted to 243 g. or made up 87.72 p. c. of the unsaponifiable matter. Time did not permit of their detailed examination.

B. The original alcoholic extract, after recovery of the solvent, having been distilled with steam to separate the volatile oil and after removal of the black resinous oily residue, was shaken first with petroleum ether to separate the fatty oil, and then with ether followed by chloroform. The aqueous layer remaining contained the water soluble constituents of the original alcoholic extract. This dilute aqueous extract was evaporated to a thick syrupy liquid.

Determination of the Amount of Reducing Sugars. The amount of reducing sugars in this extract was determined according to the

method described in *Allen's Commercial Organ.* Analysis, vol. 1, p. 418.

Wt. of sample – 3.2254 g.
11 cc. of solution reduced 50 cc. of Fehling's sol.
Percentage of sugar = 8.52 p. c.

Separation of Potassium Nitrate. 100 g. of extract were dissolved in absolute alcohol, whereupon a considerable quantity of crystals separated out. These were removed by filtration and were twice recrystallized from water. In this way 24.1 g. of an inorganic salt were obtained. The crystals were shown to be potassium nitrate by the usual tests. The absence of Na and Cl was indicated by qualitative tests.

Separation of Hesperidin. The entire extract was next dissolved in five liters of water. An appreciable amount of a dirty gray precipitate resulted which was separated by filtration. It was insoluble in water and very sparingly soluble in alcohol. About 500 cc. of alcohol were required to dissolve one-half g. of substance. Eight g. of product were obtained.

In order to purify this substance, it was heated repeatedly with alcohol until the latter ceased to become colored. Thus purified, it was of a grayish-white color and did not appear to be crystalline. It had a melting point of 250–251°. Ordinary means of hydrolysis with 10 p. c. HCl failed. The method of hydrolysis described for hesperidin in *B.* 14 (1881), 948, was next tried. This method requires that hydrolysis take place in an autoclave under pressure. Thus hydrolized a product insoluble in water resulted which was filtered from the liquid. Recrystallized from alcohol, it had a m. p. of 225°. This corresponds to the m. p. of hesperetin. Testing the aqueous filtrate with Fehling's solution, a strong reducing action was noticed.

Precipitation with Lead Acetate. After the separation of the hesperidin from the aqueous solution of the water-soluble portion of the alcoholic extract, the latter was treated with lead acetate in the usual way whereby a dense yellowish-brown precipitate was obtained. This was allowed to settle and the aqueous liquid was siphoned off.

The precipitate was again suspended in water and was allowed to settle and again the aqueous portion was siphoned off and the sludge was filtered on a Buchner funnel. This precipitate shall be known as C′.

Treatment of the Aqueous Portion with Basic Lead Acetate. The filtrate from which the lead precipitate (C′) had been separated was next treated with basic lead acetate whereby a yellow precipitate was obtained. This was treated in the same manner in which the lead acetate precipitate had been treated, namely, the aqueous portion, consisting of 12 liters, was siphoned off after the basic lead acetate precipitate had settled and then the precipitate was again suspended in water, the aqueous portion siphoned off and then the precipitate was filtered off by means of a Buchner funnel. This precipitate shall be C″.

Further Treatment of C′ and C″. Both C′ and C″ were further treated by using the same procedure. Each was suspended separately in water and H_2S was bubbled through the mixture. The PbS was filtered off. It was washed with warm water and the excess of H_2S was removed from filtrate by bubbling CO_2 through the liquid. The reddish-brown liquids were separately concentrated under diminished pressure while each of the PbS precipitates was boiled with (1) water, (2) ethyl alcohol, (3) ammonium hydroxide successively. The extracts thus obtained were set aside for further examination.

Treatment of the Filtrates From Which the Lead Acetate and Basic Lead Acetate Precipitates Had Been Removed. The combined filtrates after precipitation measured 13 liters. They were first treated with H_2S for the removal of any excess of lead acetate. The PbS was filtered off and washed several times with water. The dissolved gas was expelled with CO_2. The reddish-brown liquid was concentrated under diminished pressure to about 1.5 liters. This solution gave a positive test with Fehling's solution. The liquid was neutralized with sodium carbonate and was then made alkaline with NH_4OH. It was shaken out with (1) ether, (2) chloroform, (3) hot amyl alcohol successively.

Amyl Alcohol Extract. The amyl alcohol shakings, which amounted to about 500 cc., were distilled under diminished pressure until only 100 cc. of the amyl alcohol solution remained. This was allowed to cool whereby a large amount of a yellowish substance was precipitated, which was very soluble in water. It had a m. p. of 81°. Fehling's solution was readily reduced by it.

Isolation of Rhamnose. Eleven and two-tenths g. of the sugar resulted. An osazone was prepared by refluxing a small amount with phenylhydrazine and glacial acetic acid whereby a sticky mass was ob-

tained. This was stirred with acetone when a small number of crystals were obtained which, on purification, had a m. p. of 180°. The melting points of the substance and that of its osazone corresponds to those of rhamnose and its osazone.

After removal of the amyl alcohol from the filtrate, a reddish-brown residue was obtained which was treated with cold methyl alcohol whereby a portion went into solution. The insoluble portion was filtered off. It was of a dark brown color and was very deliquescent. It readily reduced Fehling's solution. This substance, when recrystallized from hot methyl alcohol, proved to be more rhamnose.

Isolation of Glucose. After distilling off the methyl alcohol from which the rhamnose had been removed, the resulting residue gave a strong reducing action with Fehling's solution. It yielded an osazone with a m. p. of 204–205° corresponding to that of glucosazone. A mixed m. p. with glucosazone, prepared from pure glucose, gave no depression.

The Ether and Chloroform Extracts. Nothing of interest could be isolated from the ether extract which was of a light green color and amounted to 2.3 g. The same is true of the chloroform extract which was of a dark green color and amounted to 11.2 g.

Procedure for the Isolation of Simple Natural Bases. After extraction with ether, chloroform, and amyl alcohol, the aqueous filtrate was again submitted to distillation under diminished pressure until only 250 cc. of solution remained. This was acidified with H_2SO_4 and then a saturated solution of phosphotungstic acid was added whereby an abundant precipitate was obtained. This was filtered off and washed repeatedly with water. The precipitate suspended in water was decomposed with a saturated solution of $Ba(OH)_2$ and the precipitate was filtered off. The excess of barium was removed by bubbling CO_2 through the solution. This precipitate of $BaCO_3$ was filtered off and the aqueous solution thus obtained was again distilled under diminished pressure until only about 60 cc. remained, which had the consistency of a syrup.

This syrup was extracted with alcohol. To the alcoholic washings, a cold saturated alcoholic solution of mercuric chloride was added and the mixture was allowed to stand over night, whereupon a small amount of a light brown crystalline material settled out. This amounted to 0.52 g. It was dissolved in a small quantity of water and H_2S was bubbled through the aqueous solution in order to remove the mercury. The HgS was filtered off and the excess H_2S was re-

moved by bubbling air through the filtrate. The filtrate was concentrated by distillation in vacuum and further evaporation in a vacuum desiccator, whereby a small amount of brownish crystals, 0.36 g., were obtained. They were collected on a filter and after drying had a m.p. of 234–235° which corresponds to the m. p. of betaine hydrochloride. A gold double salt was prepared which gave the following result:

0.1003 g. of $C_5H_{12}O_2N\ AuCl_4$ yielded 0.0429 g. of Au.
Theoretical 43.14 p. c. of Au. Found 42.99 p. c.

On treating the alcoholic washings of the above with a 5 p. c. solution of chloroplatinic acid, no precipitate was obtained, showing the absence of choline.

The absence of purine bases and arginine was indicated by nonformation of a precipitate when $AgNO_3$ and mercuric nitrate respectively were added to a small portion of the original solution which had been acidified with HNO_3.

. . . . . .

The solutions resulting from the decomposition of the lead acetate and basic lead acetate precipitates (C′ and C″) were evaporated under diminished pressure as previously stated. The syrup which was thus obtained reduced Fehling's solution readily. The sugars present had very likely been occluded by the lead precipitate.

Tannin Determination. The amount of tannin in the extract was determined by the hide powder method described in the *Jr. of the Am. Leather Chemists Assn.* 16 (1921), p. 113.

(Sample 1) Wt. of residue obtained from 100 cc. of solution = 0.3547 g.
Wt. of residue obtained from 100 cc. of solution after treatment with hide powder = 0.0614 g.
Percentage of tannin 17.31 p. c.

(Sample 2) Wt. of residue obtained from 100 cc. of solution = 0.3876 g.
Wt. of residue obtained from 100 cc. of solution after hide power treatment = 0.0618 g.
Percentage of tannin 17.65 p. c.

Sugars. In order to effect a separation of the sugars and other constituents present, precipitation with $Ba(OH)_2$ was resorted to. The precipitate thus obtained was of a blood-red color. It was filtered

off and, after washing with water, was decomposed with CO_2. The $BaCO_3$ resulting was filtered off and washed with water. The filtrate thus obtained was evaporated to a syrupy consistency.

The filtrate from the barium precipitate was treated in a similar manner. It was decomposed with CO_2 and the $BaCO_3$ resulting was removed. This filtrate was of a dark red color, and was, likewise, evaporated to a syrup. This syrup contained the sugars. An osazone having a melting point of 205–206° was obtained.

Separation of the individual constituents by means of solvents was next attempted.

The syrup containing the sugars was treated with methyl alcohol. The precipitate thus obtained was filtered off. The substance merely charred when heated. It was of a light brown color and its solution in water, in which it was very soluble, was dark brown. There was no precipitation with dilute H_2SO_4 for it was thought that this substance might be inorganic (some Pb or Ba compound). It reduced Fehling's solution. An ash determination yielded the following results:

Wt. of Sample	*Wt. of Ash*	*Percentage of Ash*
0.2380 g.	0.0928 g.	38.99 p. c.
0.2295 "	0.0933 "	40.69 " "

Intumescent Substance. To the filtrate obtained by treating the sugar syrup with methyl alcohol, acetone was added, producing an orange-colored, flocculent precipitate. Separated by filtration, this proved to be very deliquescent. When dried, it gave a dark reddish-orange powder. Heated on the blade of a spatula, it was found to be intumescent. An ash determination yielded:

Wt. of Sample	*Wt. of Ash*	*Percentage of Ash*
0.1244 g.	0.0362 g.	29.09 p. c.
0.0823 "	0.0242 "	29.52 " "

An attempt to remove the inorganic elements was made by triturating the intumescent substance in a mortar with aqueous HCl. The reaction mixture was steam distilled in the hope that the underlying compound might be volatile and thus be removed. However, no tangible volatile products were obtained. The acid contents of the flask were evaporated to dryness and the solid residue was extracted with hot methyl alcohol. From this solution acetone again precipitated an intumescent substance of which 0.2388 g. yielded 0.0697 g. of

ash = 29.18 p. c. Hence the acid had not removed any of the inorganic elements.

The original intumescent substance was soluble in water, methyl alcohol, and ethyl alcohol; insoluble in acetone, ether and petroleum ether. In aqueous alkali it dissolved with a blood-red color. Its acid solutions are yellow. An attempt to prepare an acetyl derivative yielded no satisfactory results.

After removal of the intumescent substance, most of the methyl alcohol and acetone were removed by distillation, the rest being allowed to evaporate spontaneously. A dark brown syrup was obtained. An osazone which had a m. p. of 205–206° was prepared from a small amount of the syrup. This was evidently glucosazone, hence the sugar may be glucose. An ash determination of the syrup was made with the following results:

Wt. of Sample	*Wt. of Ash*	*Percentage of Ash*
1.1217 g.	0.1007 g.	8.97 p.c.

After precipitation with $Ba(OH)_2$ and subsequent decomposition of the precipitate with CO_2 (see Sugars), the liquid was evaporated to dryness and the residue examined. It consisted of a dark brownish-red powder which was soluble in water. With ferric chloride, it gave a black color. However, unlike tannin, it was insoluble in ethyl acetate and did not give results with hide powder. Fusion with NaOH yielded no products which could be identified.

Phytosterolin. The upper oily or resinous mass which resulted after the volatile oil had been removed from the concentrated alcoholic extract by steam distillation after the partly aqueous, partly oily residue "A," was shaken out with petroleum ether to remove (A_1), fatty oil and with ether to remove (A_2) resinous substances. The residue (A_3) was dissolved in hot alcohol. Upon cooling, crystals separated. After a number of recrystallizations, 10.4 g. of substance remained.

The compound gave a positive Liebermann-Burchard reaction for phytosterol, also a positive Molisch test for carbohydrate. The purified substance had a m. p. of 279°. The same m. p. was found for all fractions. The substance was soluble in methyl, ethyl, amyl alcohol, also in pyridine.

It was thought that this substance was a phytosterolin so that an attempt at hydrolysis by using the method of Power and Salway [1]

[1] *Chem. Soc. J. Trans.*, 103 (1913), p. 399.

was made, but it gave negative results. The phytosterlin was next subjected to hydrolysis under pressure. This was accomplished by heating in an autoclave. The phytosterolin was dissolved in amyl alcohol and then 15 cc. of 10 p. c. hydrochloric acid were added with sufficient alcohol to make the two layers miscible. After heating for six hours, steam was passed through the mixture to remove the amyl alcohol. The contents of the flask were filtered off and the resulting solid was recrystallized from alcohol. It had a m. p. of 246° and gave a positive Liebermann-Burchard reaction. It was thought that this might be a mixture, hence it was extracted with ether for the removal of phytosterol while the original substance would remain undissolved. The substance thus obtained had a m. p. of 259° after repeated recrystallization from alcohol. It gave a positive Molisch test and a positive Liebermann-Burchard reaction. The portion insoluble in ether had the same m. p. as the original substance, namely 279°. The acid filtrate, after removal of the solid material, was neutralized with sodium carbonate and evaporated to dryness. The residue thus obtained was extracted with absolute alcohol and this solvent was evaporated. The small amount of brownish substance, which remained after this treatment, was taken up with water and treated with Fehling's solution. The test was negative.

An acetyl derivative of the original substance was prepared by heating with 20 cc. of acetic anhydride and 2 g. of anhydrous sodium acetate. The mixture was thrown into a large volume of water. The precipitate was filtered off and recrystallized from a mixture of petroleum ether and chloroform. It had a m. p. of 167–168°.

COMPARISON OF CONSTITUENTS ISOLATED FROM

MENTHA AQUATICA	MENTHA PIPERITA
	Inorganic
Potassium nitrate	Potassium nitrate
Potassium chloride	
	Hydrocarbons
Dotriacontane $C_{32}H_{66}$	Hydrocarbon resembling $C_{31}H_{64}$
	Monhydroxides
Phytosterol m. p. 133 to 134°	Phytosterol m. p. 134 to 135°
"Aquaticol" m. p. 273°	Phytosterolin m. p. 273°
Lupeol	

	Trihydroxides
———	Glycerol
x x x	x x x
Formic acid	———
Butyric acid	———
Hexylic acid	———
Heptylic acid	———
Myristic acid	———
Palmitic acid	Palmitic acid
Stearic acid	Stearic acid
———	Acid $C_{18}H_{36}O_2$?
Acid $C_{25}H_{50}O_2$	———
Melissic acid	Melissic acid
x x x	x x x
Oleic acid	Oleic acid
x x x	x x x
Linolic acid	———
x x x	x x x
Linolenic acid	Linolenic acid
	Penthydroxides
	Hesperetin
———	Hesperidin
	Hexahydroxides
Succinic acid	———
Rhamnose	Rhamnose
	Heptahydroxides
Glucose	Glucose
———	Hesperidin
	Monamides
Methylamine	———
Choline	———
Betaine	Betaine
	Unclassified
A flavone-like substance	———
———	An intumescent substance

A NOTE ON THE DETERMINATION OF IRON IN BASHAM'S MIXTURE

By John C. Krantz, Jr.

THE TENTH revision of the Pharmacopœia established standards for the ammonia (NH_3) and iron (Fe) content of Basham's Mixture. The official requirement for iron is: not less than 0.16 Gm. and not more than 0.20 Gm. Fe in each 100 cc.

Following the general procedure of the Pharmacopœia in the determination of trivalent iron, the iron content of this preparation is determined iodimetrically. In the application of this method to this preparation, a portion of the solution is evaporated to dryness and ignited. This is treated with concentrated hydrochloric acid and solution of hydrogen peroxide and again evaporated to dryness. This residue is dissolved in hydrochloric acid and water and subjected to the usual treatment for the iodimetric assay of trivalent iron. The evaporation and ignition of this liquid containing considerable quantities of sugar and glycerin is a tedious and prolonged process.

In the determination of the influence of light upon the stability of Basham's Mixture the author found the gravimetric determination of the iron as ferric oxide to be less cumbersome and more rapidly carried out than the volumetric process. The following procedure was employed:

Transfer 10 cc. of the solution accurately measured to a beaker of about 150 cc. capacity. Dilute with 40 cc. of distilled water. Heat to about 60° C. and add 10 cc. of solution of ammonium hydroxide. Boil the mixture for one minute and collect the precipitated ferric hydroxide in a tared Gooch crucible. Wash with hot water, ignite and weigh as ferric oxide. Each gram of ferric oxide obtained corresponds to 0.6994 Gm. Fe.

A sample of Basham's Mixture was prepared from tincture of ferric chloride which contained 4.53 per cent. of iron. Thus each 100 cc. of Basham's Mixture prepared from this should contain 0.181 Gm. Fe in 100 cc. as 4 cc. of tincture of ferric chloride prepare 100 cc. of the mixture. The product was subjected to assay for iron by the foregoing method and the following results obtained. The filtrate from the precipitated ferric hydroxide did not give a positive reaction with potassium ferrocyanide after acidifying with hydrochloric acid.

No.	*Grams Fe_2O_3 Weighed*	*Grams Fe in 100 cc. of Solution*
1	0.0251	0.176
2	0.0254	0.178
3	0.0260	0.182
4	0.0253	0.177
5	0.0250	0.175
6	0.0261	0.183
7	0.0256	0.179
8	0.0246	0.172
9	0.0250	0.175
10	0.0243	0.170
11	0.0250	0.172

The arithmetical mean of this series of determinations is 0.176 Gm. Fe.

Conclusion

The gravimetric method for the determination of iron in Basham's Mixture is more rapid and less cumbersome than the iodimetric procedure of the Pharmacopœia. The results obtained by the method herein outlined are concordant and sufficiently accurate for a determination of this character.

NOTES ON TESTS FOR PEROXIDES

By Charles C. Pines, B. S.*

IN THE COURSE of investigations as to the quality of commercial ether (Leffmann and Pines, *Bull. Wagner Free Inst., Sci.,* 1930, *5,* 3; also *Amer. J. Pharm.,* 1930, *102,* 58) comparisons were made between three of the generally used tests for peroxides. Peroxides are not common in the better grades of commercial ether, especially those intended for anesthesia, but the anhydrous ether furnished for analytic purposes was found to contain notable amounts in some cases. The three tests commonly employed are chromic acid, vanadic oxide dissolved in sulphuric acid and a mixture of equal parts of cadmium and potassium iodides. The last named is prescribed by the current U. S. Pharmacopœia.

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The chromic acid test, used often in qualitative analysis for the detection of minute amounts of chromium is eminently suited for detection of peroxide in ether, as ether is used for the purpose of dissolving the substance resulting from oxidation by the peroxide. Moreover, the reagent (potassium dichromate solution rendered strongly acid with sulphuric acid) can be easily prepared in any laboratory. The solution used in the tests here reported contained 1 grm. of potassium dichromate and 5 cc. of strong sulphuric acid in 100 cc. of water. To get the best results the reagent should be poured *through* the ether, a few cc. of the sample to be tested are placed in a test-tube and about 2 cc. of the reagent poured in. The latter at once collects at the bottom of the tube, but in passing through the sample the reaction occurs, and the other will become distinctly blue in a few seconds, even if the amount of peroxide present is very small. It is necessary to shake the tube only very slightly.

The vanadic test is of minor value. It is prompt and fairly delicate but the reagent is expensive.

Potassium cadmium iodide is directed by U. S. P. X. It is to be prepared freshly, using equal parts of the iodides and making a 10 per cent. solution. By keeping the solution in the dark it remains fully active for a considerable time. It is directed that the reagent should be mixed with the sample and occasionally agitated during an hour in the dark. The test depends on the liberation of iodine by the peroxide. Experiment has shown that the addition of starch will materially increase the delicacy of the reaction and avoid the tedious process of the Pharmacopœia. This was first noted by the use of starch-paper, as stated in the communication above quoted, but starch solution is much more satisfactory. The starch solution used was preserved by the addition of oil of cinnamon, as suggested by Professor F. X. Moerk.

A solution of .5 grm. mercuric iodide and 2.5 grm. of potassium iodide in 50 cc. of water with addition of starch solution, gave very satisfactory results. A solution of one drop of U. S. P. X hydrogen peroxide in 100 cc. of distilled water was made and about 10 cc. of this tested with the mercuric solution. A marked purplish blue tint was developed in five minutes. Neither potassium cadmium iodide nor the mercuric solution give any color with the aldehydic compounds in commercial ether.

THE PHARMACOPŒIA AT WORK

By E. Fullerton Cook

Chairman of the U. S. P. X Committee of Revision

The Pharmacopœia and the Physician.

THAT PHASE OF THE MEDICAL sciences usually spoken of as "treatment" still occupies an important place in the service rendered the sick by the doctor in practice. Diagnosis is essential and today is being properly emphasized in the training of physicians; surgery is usually a last resort but no one would belittle the value of this medical specialty when the conditions demand the surgeon, but between these two lies a vast field of opportunity and need, herein is the hope of most of the sick and the future of many thousands of dependents.

The products of the earth have been sought and tested in a search for the cure of disease and for a specific with miracle-working power. Gradually, through the centuries, honest and earnest students have accumulated facts concerning the remedial action of drugs and some of these medicines are among our most valued heritages.

Most will agree that the successful "treatment" of disease is the doctor's biggest and most difficult problem. Here science has not yet fully met the need although no world problem is today being more earnestly studied than this and no finer scientific equipment or greater financial backing has been supplied in any field than is now at work upon the maintenance or restoration of health.

Recently an honest physician, one of the greatest of our time, stood by the sick bed of a child; that dread disease pneumonia had ravaged the frail body for days; every available remedy had been tried but the toxines had gradually gained mastery and as he turned away with no hope he said "grant that some day we may learn how to combat this disease; we know little about it now." But to the honor and glory of the medical sciences there are credited many other victories, and the control of many diseases are even now within their hands.

Today in the Pharmacopœia many remedies are found which, when skilfully employed, by those who are trained and who are given the opportunity, approach that miracle-working power which has been the dream of the ages:

Among these official products are

Ether, Chloroform and Nitrous Oxide, all general anesthetics without which modern surgery would have been impossible.

Cocaine, Eucaine Hydrochloride, Procaine Hydrochloride, Ethyl-aminobenzoate, Ethyl Chloride and other local anesthetics making possible painless minor operations, and teeth extraction.

Phenol, Cresol, Mercuric Bichloride, Hydrogen Dioxide, Iodine, Dakin Solution, Chloramine, Dichloramine, Silver Nitrate, Silver Proteinates, Yellow Mercuric Oxide, Ammoniated Mercury, Sterilization Methods and other combatants of bacterial infection are official. These agents are the right hand of the surgeon and the practicing physician and the world acknowledges its debt to Pasteur and Lister and other pioneers who dared to try these products and had the wisdom to interpret their results.

Diphtheria Antitoxin, Tetanus Antitoxin and *Smallpox Vaccine* —what power to save life and prevent disease rests within these marvelous products. But a few years ago a death stalked the earth which these now successfully control in large degree. A new Pharmacopœia will doubtless include later developments of the same type of remedies and protectants.

Cinchona and *Quinine,* official in more than a dozen forms, would alone make the Pharmacopœia famous if familiarity did not cause forgetfulness of the blessing they bestowed on the human race through the elimination of one of the world's most distressing diseases.

Ergot and *Pituitary* and their preparations are important remedies in the hands of those who know their use.

Santonin, Oil of Chenopodium, Aspidium, Carbon Tetrachloride, Pelletierine, etc., have a world-wide application. They are the foundation of the treatment for restoring health to whole nations and races in the elimination of hookworm and other parasitic diseases.

Digitalis, Strophanthus, Squill and their preparations, *Quinidine Sulphate, Amyl Nitrite, Sodium Nitrite, Spirit of Nitroglycerin, Nux Vomica* and *Strychnine, Aconite, Epinephrine* and other drugs with specific action upon the heart are often the means for saving and prolonging life.

Acetanilide, Acetphenetidin, Antipyrine, Amidopyrine, Acetylsalicylic Acid, and other salicylates, etc., a group of synthetic products which are analgesic and antipyretic in action and employed today to an unbelievable degree by the doctor and the public.

The *Bromides* in all their forms are valued remedies under distressing conditions and find a real place in the useful materia medica.

Barbital, Phenobarbital, Carbromal, Sulphonmethane, Sulphonethylmethane, Chloral Hydrate and other products of the "newer materia medica," from the laboratory of the synthetic chemist, are remedies which find a place in medical treatment often of first importance.

Chaulmoogra Oil and *Ethyl Chaulmoograte*—are the first hope offered in the age-old fight against leprosy.

Opium, its preparations and *its alkaloids, Morphine* and *Codeine* are by some thought of only as a curse upon the race but in pain and tragic suffering they daily bring relief and life-saving rest to thousands while passing through some crisis of life.

Belladonna, Hyoscyamus, Stramonium, Pilocarpus, their preparations and their alkaloids *Atropine, Hyoscyamine Hydrobromide, Homatropine Hydrobromides, Scopolamine Hydrobromide, Physostigmine,* etc., all find a place in modern medicine because of their many important physiologic actions, including the mydriatic or myotic effect upon the pupil which makes possible scientific eye examinations and treatments.

Arsphenamine and *Neoarsphenamine* are Pharmacopœial products which are outstanding examples of that combination of science and medicine, chemo-therapy, whereby it is hoped that the last dread disease may yet be conquered.

The great varieties of *Iron, Mercurials* and *Iodides*—are remedies of varying degrees of importance but each occupying its own place in treatment.

Cod Liver Oil, especially deserves recognition for its unique service in health restoration under special conditions only recently understood.

Thyroid and *Thyroxin* find a legitimate place in modern medicine and this class of essential harmones are slowly yielding their secrets to scientific study. Insulin is but one illustration of what may be anticipated.

Cathartics and Laxatives of every variety are official. Would you believe that there are actually forty-seven varieties in the U. S. P. X.? Not one need for a proprietary or a specialty in this class.

Emetics—Seven are official including *Ipecac, Tartar Emetic* and *Apormorphine Hydrochloride.* Stomachics—thirty-nine bitters or

carminatives now in the U. S. P. X., a varied and useful selection for any doctor;

The *Digestants*—include *pepsin, pancreatin,* and *oxgall;*

Expectorants—there are thirty-seven kinds, among them *Senega, Terpin Hydrate, Creosote, Creosote Carbonate, Guaiacol, Guaiacol Carbonate, Terebone,* etc., etc.

Diuretics, these include three *Acetates,* three *Citrates, Caffeine* combinations such as *Caffeine Sodio-benzoate, Theobromine Sodio-salicylate,* etc.

There are *Parasiticides,* twelve *Acids,* twenty-four *Antiacids,* also *Protectives,* including four *Bismuth Salts, Demulcents,* twenty *Emollients,* thirty-six *Astringents,* eight *Counter-irritants,* ten *Antispasmodics,* and many other remedies not mentioned, together providing over six hundred Pharmacopœial selections for the use of the doctor.

This would seem to be a formidable list of remedies for any one physician to gain intimate experience with, but here enters the nation-wide application of the Pharmacopœia; it is not for local use, its aim is to meet the needs of every doctor of every class and preference.

But with greatly varied choice, a selection representing the best judgment of a group of therapeutic experts, and chosen without favor or pressure from all avoidable material medica, why do not these Pharmacopœial products stand all sufficient and alone among world remedies?

Essentially they do, notwithstanding the belief of many to the contrary.

In the Charter's Report study about 72 per cent. of all remedies prescribed by physicians in 17,000 representative prescriptions, from every section of the country, were official in the U. S. P. X; in a study by the writer in twenty-five cities of the United States two years ago, from California to Maine, 72.9 per cent. of the ingredients in 12,000 prescriptions were official in the current Pharmacopœia; among the ingredients in the many hundreds of formulas standardized within the last two years by the American Drug Manufacturers Association, over 82 per cent. are now U. S. P. substances; a study of the formulas in the catalogue of the largest physicians' supply house in America, formulas which must represent the demands of American doctors, show about 73 per cent. of the

ingredients to be Pharmacopœial, and finally a tentative analysis this year of 19,000 prescriptions, made by a committee making a national survey, indicates 82 per cent. of U. S. P. ingredients among those prescribed. Such statistical evidence indicates the importance and value of the present U. S. P. therapeutic agents in medical treatment and the extent to which they are known and demanded by the physicians of today.

True the doctor does not often own or use a Pharmacopœia as such but up-to-date treatises on therapeutics, books like "Useful Remedies" of the A. M. A.; Fantus on "The Technique of Medication;" the Courses in Pharmacology and Therapeutics of the medical schools, the A. M. A. "Epitome of the U. S. P. and N. F." and even the representatives of pharmaceutical manufacturers carry many U. S. P. drugs to the doctor, though they may sometimes be in other than official form or combination.

It is not surprising that all medicines used are not in exactly the U. S. P. form. There are many reasons for this: The U. S. P. contains but one tablet, the "bichloride tablet," and yet tablets are a popular form of medication today. But here the U. S. P. is serving an essential service for it standardizes most of the remedies entering these tablets. The same is true of *capsules* and *ampuls,* both extensively used and popular forms of medication. Shall the U. S. P. extend its titles to cover the thousands of varieties of tablets, capsules and ampuls in use or is it fulfiling its purpose by holding up the standards of strength and purity for the ingredients entering these?

Another potent reason for the manufacturer adopting other than U. S. P. forms of medication is the fact that all U. S. P. preparations are necessarily on a price-competitive basis which renders them more or less unprofitable items to sell. This is an economic situation which must be recognized and corrected, if possible. "Quality" rather than "price" should dominate the selection of medicines, but, once again, if all manufacturers claim to meet the U. S. P. standard the quality argument disappears and price dominates to the disadvantage of those most conscientious and careful.

Still another influencing factor in the adoption of a specialty, even though that may practically parallel an official product, is its control through a trade-marked title and the many advantages this offers to the owner. Neither is it likely that when the Food and

Drugs Act was proposed and passed in 1906 that any of its enthusiastic advocates foresaw the possibility of manufacturers finding it advantageous to promote other than U. S. P. and N. F. products and thus avoid the legal control of standards yet that is another of the influences back of the medical "specialty" of today.

The Pharmacopœia and the Pharmacist.

Conditions peculiar to the period in which we live have also influenced the extent to which the average retail druggist uses the U. S. P. Note the qualifying word "average" for there are many pharmacies where even now the Pharmacopœia is in daily and continuous use. When the pharmacist is filling many prescriptions, when he is still making some of his preparations and especially when he tests any of them for purity or strength, the Pharmacopœia is his constant book of reference. Go into the pharmacies of thousands of prescription pharmacists throughout the United States and it will be found that they do not question the need for or the value of the U. S. P. X. Naturally those who practice little pharmacy have little need for a Pharmacopœia and no change in its scope or treatment would make it of greater use to them.

The Manufacturer and Chemist Use the Pharmacopœia.

Only more details in processes or tests or assays or perhaps an enlarged scope would make the U. S. P. a book of greater value than the present edition, to the manufacturer of pharmaceutical or chemical products or to the chemist, private or governmental, who is checking and controlling the standards of medicines, that they may comply with the official requirements. In this field splendid and practical co-operation in revision is now available.

Colleges of Medicine and Pharmacy.

The colleges too are using and benefiting from the U. S. P. and few criticisms but much praise of the U. S. P. X has come from this source. Practically every medical college in the United States is using the U. S. P. X directly or indirectly as the basis for their courses in pharmacology and therapeutics.

The following paragraphs are quoted from a letter sent in 1927 by the Sub-Committee on Therapeutics of the Committee of Revi-

sion to the professors of therapeutics in every medical college in the United States:

"As you know, the immediate purpose of the Pharmacopœia consists in providing standards for the standard drugs, and in this it may be truthfully said to reflect the best practice of the American Medical and Pharmaceutical professions. By giving official recognition, sanction and encouragement to the best, it serves as a powerful incentive and means for improvement and progress of the two professions who own it in common, and who manage it by a democratic system that should and does make the Pharmacopœia representative of, and responsive to, the whole membership of both professions.

"The selection of the 'Best' in drugs is necessarily a delicate undertaking; but the Committee tried faithfully to act in harmony wtih the tendencies of modern medicine; to eliminate what seemed at present useless or practically superfluous; and to add the new drugs whose value had been fairly definitely established. This was made possible by the authorization to admit drugs protected by patent, as is the case with so many of the synthetic chemicals. Accordingly, the present Pharmacopœia was able to include standards, and incidentally non-copyrighted names; for the arsphenamines; procaine (novocaine) and other synthetic anesthetics; chaulmoogra oil and ethyl chaulmoograte; amidopyrine (pyramidon); the colloidal silver preparations, mild and strong; barbital (veronal) and phenobarbital (luminal); calcium iodobehenate (sajodin); carbromal (adalin); chloramine (chlorazene) and dichloramine; epinephrine (adrenalin); thyroxin, and a number of others. To an increasing extent, teachers and students may find it profitable to look upon the titles of the Pharmacopœia as a basic reference list of drugs and preparations of worth; but even those who may not agree with the Committee in all its decisions will find the list of additions and deletions at least quite interesting. Incidentally, strict adherence to the official names and abbreviations helps to avoid confusion in prescribing and in dispensing.

"The bulk of the text of the Pharmacopœia consists of working directions for preparations and for testing, which are very important to pharmacists and indirectly also to physicians, since they insure uniformly high quality of the drugs; but the details of much of this text are not in the province of medical men. There are, however, quite a number of other valuable features, which make the Pharmacopœia a very handy source of useful information. These are best appreciated by examining the table of contents, on pages III and IV of the book, or better still, by running through its pages. We would mention especially the authoritative definitions and descriptions; the physi-

cal constants such as solubilities, melting points, etc.; the admirable succinct 'Identification Tests for Chemicals,' pp. 440-444; the descriptions of standard analytical procedures and methods; the formulas for test solutions and volumetric solutions and equivalents; the tables of formulas and molecular weights of a large list of chemicals; of equivalents of temperatures, of weights, and of measures—all in convenient form and reliable. The descriptions of the bio-assays are of especial interest to pharmacologists. It is interesting to recall that the United States Pharmacopœia has set the pace for the world in this subject."

Pharmacy Colleges almost universally use the U. S. P. and N. F. as the basis of instruction and require the students to purchase copies as textbooks and laboratory manuals.

The Policy on Scope.

As the Scope of the Pharmacopœia, which covers both the articles included and the treatment they receive in the text, is of first importance in establishing the value of the book, it is proper to again refer to the principles determining such decisions.

There is much misunderstanding about this question, primarily through a lack of full information. The unit of measurement is not the size of the book or the number of titles, it is one of principle.

Three criteria formed the basis for admissions in the U. S. P. X. They were: *first,* therapeutic value, *secondly,* sufficient use by physicians and *thirdly,* those substances required for the manufacture or standardization of accepted therapeutic agents. There cannot be a serious departure from these fundamental principles if our Pharmacopœia is to deserve the respect of the authorities in modern medicine and pharmacy. However, there seems little disagreement on these principles, and no one who is scientific or progressive in spirit would want our Pharmacopœia to retrogress.

The question becomes one of the application of old principles rather than the adoption of new ones. The medicinal substances seeking admission must present either or both of two qualifications, value and use.

The Committee of Revision is composed of experts in the various medical sciences, there are chemists in a half dozen special fields, botanists, pharmacognocists, bio-assayists, pharmacists, therapeutists, serologists, bacteriologists, physicists, etc.

Now who are the experts to determine admissions and deletions? The physicians in the Convention and on the Committee have asked that the responsibility for deciding therapeutic value be placed upon the medical profession as best qualified to judge. This is their chief contribution to the revision. In determining the extent of use of drugs the prescription pharmacists have a genuine contribution to offer and that this side of the scope discussion might be properly presented the Chairman appointed five pharmacists as members of the Sub-committee on Scope.

These members were George M. Beringer, A. G. DuMez, C. H. LaWall, Leonard A. Seltzer, W. H. Zeigler. They had a vote on every question before the sub-committee and actively participated in the discussions.

One of the first questions before the U. S. P. X Committee of Revision, as it was organized in 1920, was this one of "Scope Policy." After an extended discussion, first in conference and then by correspondence, the general committee by a mail vote of 2 to 1 placed the final decision, in those instances in which recommendations of the scope sub-committee were questioned, in the hands of the physicians when the question was one of therapeutic value and use, and the final decision with the pharmacy groups as to the selection of substances needed for manufacturing or standardizing.

In the previous Pharmacopœia, the U. S. P. IX, the executive committee voted on all admissions and deletions, after the sub-committee on scope had submitted their report, and changed many of the sub-committee's recommendations. This was unsatisfactory to the medical profession since only two of the fifteen members of the executive committee were practicing physicians.

The pharmacy group therefore largely controlled the scope of the U. S. P. IX and 243 titles were deleted. The medical members were primarily responsible for scope in the U. S. P. X when 191 titles were dropped. Neither policy has proven satisfactory to all.

Perhaps out of this experience of two decades a better way can be developed. Professor Arny in a recent article* suggested a plan which seems to possess the merit of entire fairness, and introduces a well-established democratic principle which could apply to the reports of all experts, giving all groups a free hand to fully express

* American Druggist, Oct. 1929 (page 51).

to the committee their judgment but still retaining a controlling vote within the general committee, if it does not agree with the conclusions.

This plan would retain the present custom of placing all sub-committee reports, including scope, before the general committee for their criticisms and suggestions, but with an added agreement that members of the committee, for an adequate reason, may call for the reconsideration of any detail of a report. However, the reversal of any recommendation of a sub-committee shall require the approval of at least two-thirds of the general committee.

This suggestion to adopt a two-third vote to change the decision of a group of experts is but following the precedents of our national government.

The Personnel of the Board and Committee on Revision.

Another decade has almost passed and within a few months the Decennial Convention will assemble in Washington to determine the "General Principles" which shall govern the next revision and to elect the officers, trustees and committees who shall carry out its mandates for the next decade.

The Board of Trustees controls the business of the convention in the years between its adjournment and its reassembling. The reports of the chairman and secretary of the board at the convention will evidence the able manner in which these duties have been performed for the past decade. Those who are experienced and tried in executive and responsible office are always selected by the convention for service as pharmacopœial trustees, involving as it now does, relatively large trust funds.

The need for a committee of revision composed of those who have demonstrated their technical qualifications by actual published researches or creative work in the subject they represent, is self-evident.

The present revision has offered a unique opportunity for those interested in the U. S. P. to demonstrate their qualifications for a place on the new committee. In addition to those who are now members of the Committee on Revision and who have had ample opportunity to prove their qualifications, each sub-committee chairman was given the privilege of nominating auxiliary members of his

sub-committee from those who were not on the committee but who, in his judgment would be helpful. A list of these auxiliary members, and many others who voluntarily helped in the revision, will be found on pages lv and lvi of the U. S. P. X.

One of the objects of this plan was to encourage and develop workers in pharmacopœial revision and, all things considered, the personnel of the new committee should be chiefly made up of these workers who have already proven their ability and, even more important, their possession of that somewhat intangible quality "willingness to give of time and strength and knowledge," in a largely voluntary service, but where high idealism prevails.

Pharmacopœial history in our generation is rich in its record of service from workers of this type, such men as Rice, Diehl, Sheppard, Charles E. Dohme, Whelpley, Remington, Beringer, Lyons, Francis, Kraemer, Thompson, Oldberg, Hallberg, Chas. Caspari, Jr., Horatio C. Wood, Sr., Prescott, Ebert, Wilbert, Bedford, Maisch, Seasby, Wenzel, and dozens of others.

These possess those sterling qualities of integrity, industry, thorough training and willingness to give of their time and strength, and no other qualification can justify a place on the Committee of Revision if these are missing.

MEDICAL AND PHARMACEUTICAL NOTES

THE TOAD IN MEDICINE—The venom of toads, for centuries used in Europe as a source of poison and in China as a medicine, contains potent principles that resemble drugs in therapeutic use today and may provide medicine with new weapons against heart disease.

Four kinds of chemical substances have been isolated in crystalline form from Ch'an Su, dried toad venom used as medicine in China for hundreds of years. The researches were conducted by Drs. H. Jensen and K. K. Chen of Johns Hopkins.

Dr. Chen is a Chinese biochemist whose research on an old Chinese drug plant gave modern medicine the drug ephedrine, which has come into wide use in the treatment of hay fever and colds.

In the river and lake regions of China is found a large toad which, when irritated, secrets a whitish, slimy venom from glands located behind the eyes. The Chinese have long used this dried venom in treating canker sores, sinus trouble, inflammations, toothache and bleeding gums.

The reason why the toad venom is effective for stopping bleeding and promoting drainage of infected sinuses was explained when Drs. Jensen and Chen isolated from the venom two principles which raised blood pressure, one of them identical with epinephrine or adrenalin, the principle of the suprarenal gland in animals.

But the poisonousness of toads is explained by the isolation of two toxic principles in the toad venom that have a pharmacological action quite similar to the familiar digitalis glucosides used in treating heart trouble. One of these, cinobufotoxin, as it is named in honor of its origin and toxicity, is so potent that one-thousandth of a gram would kill an ordinary cat. The other poison in the Chinese toad venom, cinobufagin, is not so powerful.

These poisonous principles explain the cause of death of the husbands of marriage-weary Roman women who fed their mates toad lungs.

Other poisons of animal origin are snake venom and poisons from fish, scorpions, spiders, bees, ants, beetles and other insects. In common with gland extracts such as thyroxin, adrenalin, pituitrin, and

insulin, these poisons are toxic in large amounts, but sometimes beneficial in small doses.

Close chemical relations between toad poisons, digitalis, bile acids, cholesterol, ergosterol, the vitamin D substance, and perhaps the female sex hormone are suggested by Drs. Jensen and Chen and may guide their use in the treatment of disease.

TRANSMUTATION OF THE ELEMENTS A FACT—Changing one chemical element into another by the action of a third element and in the process obtaining two still different elements is the atomic juggling described to the American Chemical Society by Dr. William D. Harkins of the University of Chicago, and Dr. Arthur E. Schuh of the Bell Telephone laboratories.

The experimenters were not able to obtain changed elements in any useful quantities, but have been working with single atoms, observed by the indirect process of watching the cloud of fog they leave behind them as they dash through a chamber containing water vapor at low pressure.

Nitrogen, the element that makes up some three-quarters of the air we breathe, was what they started out with. It was bombarded with alpha particles—nuclei of helium atoms given off by thorium, an element like radium, while disintegrating into another element. There is no way of aiming the atomic bullets, but after a long enough series of trials an occasional hit may be scored.

Dr. Harkins and his associate studied nearly half a million tracks of atoms, and only found two that showed evidence of a disintegration of the atoms into another element.

Here is the complicated series of events they believe to take place in the instant of time that the change requires:

The alpha particle, or helium nucleus, attaches itself to the nucleus of the nitrogen atom. It thus becomes the nucleus of an atom of fluorine. In less than a millionth of a second, however, the fluorine nucleus emits a fast hydrogen particle, or proton, part of the atomic nucleus. The remaining part is the nucleus of an oxygen atom of mass 17. Ordinary oxygen has an atomic weight of 16, but it has a variant, or "isotrope" of atomic weight 17.—(*Science Service.*)

IODINE IN KENTUCKY RAIN—Where does iodine in Kentucky rainwater come from? Dr. J. S. McHargue and Dr. W. R. Roy, of the Kentucky Agricultural Experiment Station, asked their fellow-chemists this question at the recent meeting of the American Chemical Society, but did not offer to answer it.

Iodine in natural waters of inland regions has figured importantly in public-health work since the discovery of its importance in preventing goiter. In regions near the sea it is assumed that the iodine in natural waters comes from sea-water spray flung into the air and evaporated into clouds. But Kentucky, Dr. McHargue pointed out, is 500 miles from the nearest point on the sea.

Iodine does not seem to be present as a gas in the air. Dr. McHargue made a critical chemical test of the air, bubbling it through a solution that should have detected the element if present even in minute quantities, and got no results. The source of the iodine in Kentucky rainwater remains a mystery.

However, Dr. McHargue concluded, recent investigations indicate that forage crops and vegetables grown in his State contain appreciable amounts of iodine. There are no known areas in Kentucky where goiter is more prevalent than in other parts. Apparently the iodine content of natural waters and foods produced in Kentucky is adequate for the normal growth and metabolism of animals.—(*Science Service.*)

ERGOT RESEARCH—In view of the serious loss of ergotoxine which occurs on keeping liquid extract of ergot, J. H. Burn has been experimenting with powdered and defatted ergot (*Quarterly Journal of Pharmacy and Pharmacology,* 1929, 4, 515) as a means of maintaining a sufficient concentration in the circulation. Cats were selected for the tests, and the powdered and defatted ergot was given *per os*. The amount of ergotoxine in the circulation was estimated by determining the dose required to produce a reversal of the pressor effect of adrenalin in the spinal preparation, and observing whether this differed from the dose required in normal cats. Normal cats require 0.507 mgm. per kilo, and cats which have eaten 1 gm. of ergot eighteen to twenty hours before require only 0.259 mgm. per kilo. It was calculated that a cat may absorb about 30 per cent. of the alkaloid present in 1 gm. of a good sample of ergot within twenty hours of eating it, *e. g.*, 0.75 mgm. The amount of ergotoxine in the circulation was approximately the same after forty-two hours. It is concluded that

powdered and defatted ergot, enclosed in capsules, may be used medicinally to maintain a concentration of ergotoxine in the circulation during the puerperium, an initial dose of the alkaloid having been injected under the skin after the delivery of the placenta.—F. Wokes and G. K. Elphick (*Quarterly Journal of Pharmacy and Pharmacology*, 1929, 4, 539) follow up the work of Linnell and Randle in 1927 by investigating, by means of fractional percolation, the loss of available ergotoxine in official processes for making liquid extract of ergot. A 1 in 1 extract takes out rather less than half of the total available ergotoxine. A 1 in 2 extract takes out between two-thirds and three-quarters. If percolation is continued beyond a 1 in 2 extract, the amount of ergotoxine in each fraction diminishes steadily, and the sixth fraction contains only a sixteenth of the ergotoxine present in the first fraction. The total extractive matter in these fractions diminishes much more rapidly than does the ergotoxine, indicating that there is greater difficulty in the extraction of the ergotoxine. The total solids in a liquid extract of ergot cannot be taken as any guide to the ergotoxine content. In the assay of ergot the extract prepared should be at least as dilute as 1 in 4, which may be assumed to take out about nine-tenths of the total available ergotoxine. In the case of previous assays of ergot which were based on the assumption that a 1 in 1 extract had removed all the ergotoxine, the results will require to be increased by 100 per cent. On the basis of these figures, if Polish or Russian ergots are to be rendered available for the preparation of liquid extract of ergot, the standard for this extract should be reduced from its present level of 0.05 per cent. to less than half (*i. e.*, 0.020 or 0.015 per cent.). If such a reduction was made, while it would admit the employment of some poorer ergots, the much greater yield obtainable from good ergots would give a considerable advantage to those who use them. The assistance of Stafford Allen & Sons, Ltd., is acknowledged.—(Through *Chem. & Drugg*)

ALUMINIUM ACETATE PREPARATION—F. Uratschko, in *Pharmazeutische Presse* (February, 1930, pp. 17-18), gives particulars of a method to prepare aluminium aceto-borotartrate.

Solution of aluminium acetate	100.0
Tartaric acid	1.2
Boric acid	0.75

The solution is evaporated to dryness and the resulting product can be packed in ordinary paper, thereby saving freight. Solutions are unaffected by heat and remain clear in 50 per cent. concentration. The cost is no higher than that of the official preparation.—(Through *Chem. & Drugg.*)

Tobacco and Tobacco Smoke as a Factor in Etiology of Cancer—Lickint reviews the experimental and clinical work that has been done on this problem. As yet only atypical epithelial proliferations (not true cancer) have been produced in animals by means of tobacco tar. The author calls attention to the fact that of the 4059 cases of cancer of the bronchi and the lungs reported in the literature, 3370 were in men and only 689 in women (a ratio of 5:1), and also to the increasing frequency of cancer of these organs. He believes that this is to be explained in part by the great increase in cigarette smoking, with its attendant inhalation. Not only smokers but non-smokers are exposed to this danger in smoke-filled rooms. Because of the finer state of division of the particles in tobacco smoke, they have a much greater penetrating power than have particles of dust. In the case of tobacco smoke the maximum amount of irritation is produced because, in addition to the mechanical irritation (particles of carbon), there is also a chemical (tarlike combustion products) and a thermal (current of heated air) irritation. Other investigators who believe that tobacco smoke, particularly cigarette smoke, is partly responsible for the increased incidence of cancer of the bronchi and the lungs are Perret, Joannovic, Kanngiesser, Berblinger, Fahr, Hochstetter, Ferenczy and Matolcsy and Schönherr. Because of the long time that nicotine and other products of the burning of tobacco remain in the liver and urinary bladder, the author believes that primary cancer of these organs also is sometimes caused by tobacco. The article is followed by a bibliography containing 167 references.—(*Zeitschrift für Krebsforschung,* Berlin, 30:317-448 [Dec. 16] 1929, through *J. A. M. A.*)

NEWS ITEMS AND PERSONAL NOTES

The Thirty-seventh Chemists' Exhibition, organized by the *British & Colonial Pharmacist,* will be held in the new hall of the Royal Horticultural Society, situated in the centre of the West End of London, an advantage which cannot be over-estimated, particularly where visitors from overseas are concerned. The dates are May 26th-30th. All members of the drug and chemical trades who are in England during the week will receive a cordial welcome on presentation of their professional or business cards.

ABSTRACT OF SEVENTEENTH ANNUAL REPORT OF MELLON INSTITUTE OF INDUSTRIAL RESEARCH—In his seventeenth annual report to the board of trustees of Mellon Institute, Director E. R. Weidlein has summarized the activities of the institution during the fiscal year ended February 28, 1930. The sum of $929,109.02 was contributed by Industrial Fellowship donors in support of research—an increase of $129,025 over the preceding year. The total amount of money appropriated to the institute by companies and associations, for the nineteen years ended February 28, 1930, was $6,749,273.

Throughout the entire fiscal year 71 Industrial Fellowships, requiring the services of 209 full-time research men, were in operation. Sixty-one Industrial Fellowships—21 Multiple Fellowships and 40 Individual Fellowships—were active at the beginning of the new fiscal year. Eight are being sustained by industrial associations. The industrial research personnel consists of 21 Senior Industrial Fellows, 88 Industrial Fellows, 34 full-time Fellowship assistants, and a number of part-time assistants.

Especially notable results have been forthcoming from the following investigations: Air pollution, bricklaying, carbonated beverages, cooking utensils, food varieties, heat insulation, iodine, laundering, organic synthesis, petroleum production, sleep, and vitrified sewerpipe. Ten fellowships completed their research programs: Beds, cast iron (2 fellowships), chrome plating of aluminum, gum, hats, industrial alcohol, licorice, stearic acid, and surgical supplies. Nine fellowships became active during the fiscal year: Can, fatty acid uses, garment, hemp paper, nicotine, oxygen, rosin oil, steel treatment, and

wood by-products. Five new fellowships have been accepted and their operation will be begun during the early part of the new fiscal year.

The institute's department of research in pure chemistry has continued its work on acidic carbohydrates occurring in plants and on other problems in the province of sugar chemistry.

Of the 61 Fellowships now active, 29 have been in operation for five years or more. Of this number 15 have completed more than ten years of work.

The publications by members of the institute during the calendar year 1929 included 7 bulletins, 50 research reports, and 59 other papers. Sixteen United States patents were issued to Fellows of the institute. The total contributions to the literature for the eighteen years ended January 1, 1930, have been as follows: 15 books, 96 bulletins, 528 research reports, 849 other articles, and 407 United States patents. These publications are listed in the institute's Bibliographic Bulletin No. 2 and its three annual supplements, copies of which will be sent to research directors, science teachers, and librarians upon request.

Copies of the full report are available to all interested persons.